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Perspectives in Venereology—1960

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This is the 14th of a series of annual reviews of the world's literature [this *Bulletin*, 1948, v. 23, 135–144; 1949, v. 24, 99–111; 1950, v. 25, 331–343; 1951, v. 26, 101–121; 1952, v. 27, 297–314; 1953, v. 28, 489–503; 1954, v. 29, 541–562; 1955, v. 30, 453–473; 1956, v. 31, 769–787; 1957, v. 32, 521–543; 1958, v. 33, 901–922; 1959, v. 34, 697–716; 1960, v. 35, 725–741].

Introduction

The past year has shown two significant advances. One is the proved effectiveness of metronidazole against trichomoniasis; this provides a striking systemic cure and adds a powerful stimulus for an epidemiological approach to this condition now that it can be effectively eradicated when found. The second is the adaptation of fluorescent antibody techniques to venereology, particularly to the serodiagnosis of syphilis. It appears possible that results comparable with those obtained by the complicated Treponemal immobilization (TPI) test may be obtainable by this simpler and less expensive procedure, and more accurately than by complement-fixation tests involving antigens prepared from cultivable and virulent treponemes, which so far have not quite reached the TPI test in specificity and sensitivity.

On the sombre side the cases of gonorrhoea throughout the world continue to mount—in some areas alarmingly—and in a number of countries, where early syphilis has been reduced to a low level, disquieting reverse trends are being observed with this disease also. At the same time, as a result of a false sense of security and of apathy within and without the profession, venereology itself is in danger owing to the very small number of future venereologists at present under training. That it is venereology, not the venereal disease, which was dying was the opinion of RAJAM (1959) in a plea for more study and teaching of the subject.

One of 5 volumes of a new book in German on Dermatology and Syphilology by GOTTRON and SCHOENFELD (1958) was devoted to the venereal diseases. Recent advances in the treatment of these conditions were considered by CAMARILLO (1958); GARSON (1959); KING (1959); and by EVANG and MELLBYE (1960).

Antibiotics

General

The Seventh Annual Symposium on Antibiotics held in Washington in 1959 was described by WILLCOX (1960).

Outlines of 36 different bioassay methods for 17 of the most frequently used antibiotics were presented by KIRSHBAUM and ARRET (1959). Blood and urine levels of potassium penicillin V were compared with those of sodium penicillin G by HOLLAND *et al* (1960); those of

G were initially higher and those of V were more prolonged.

HUMPHREY *et al.* (1959) described the establishment of an international unit of phenoxymethyl penicillin (V) as activity contained in 0·000590 mgm. of the international standard. An international unit of streptomycin was also defined (HUMPHREY *et al.* 1959a). That temperature affects the discs used for penicillin sensitivity tests was noted by KHALEQUE *et al.* (1960).

Penicillin salts of steroidal amines were described by BOYCE and VAIDYA (1959, 1959a). A new compound of dipenicillin G, a repository salt well tolerated and giving levels for 72-96 hours, was reported by BENVIGNATI and AVANZINI (1959). A Czechoslovakian oral penicillin preparation containing both penicillin V and G was described by KOLCAVA and DOSTAL (1958).

Laboratory studies on phenethicillin potassium 6 (α-phenoxypropionamido) penicillinate were made by MCCARTHY *et al.* (1960) and by KNUDSEN and ROLINSON (1959). Weight for weight this penicillin (Broxil) will give serum levels comparable with those of penicillin G by injection (see *Brit. Med. J.* 1959).

Reactions to Antibiotics

(a) *Toxic reactions.* Reactions of all sorts to antibiotics were considered by WELCH (1959). BOYD *et al.* (1960) noted that the medium lethal dose of benzyl penicillin in rats was 6·7 gm. per kgm. The same authors (1960a) considered nausea, vomiting, etc. as toxic side-effects in patients who were hypersensitive. BREESE *et al* (1960) described methods of increasing local tolerance of benzathine penicillin by the purification of the base and by the addition of procaine penicillin and of prednisolone.

In the chemical field 3 cases of severe reactions, one of which was fatal, meeting the criteria of the Stevens-Johnson syndrome and following the use of sulphamethoxypridazine (Kynex), were reported by SALVAGGIO and GONZALES (1959), as were 3 cases of malaise and adenopathy after the same drug by ANDERSON and WISSINGER (1959) who reported a reaction rate of 2·7% on 223 patients.

(b) *Allergic reactions.* Penicillin hypersensitivity was considered by EVANS (1959) and by TYSON (1959), and acute allergic reactions by LOGAN (1960) and by PATTERSON (1960).

16 cases of anaphylaxis in 3 years were reported by HOIGNÉ and SCHOCH (1959), and 3 fatal cases in 10 months by SCHIFF and DAVIS (1959). 7 sudden deaths following administration of penicillin were reported by MENDES *et al.* (1959) who noted that blood withdrawn from the right atrium 6-12 hours after death remained unclotted. Non-fatal anaphylaxis after administration of procaine penicillin was reported by LOGUE and BARRETT (1959) and a personal case by PUTNOI (1959). BJORNBERG and SELSTAM (1960) recorded 33 acute psychotic reactions following the use of procaine penicillin which presumably had been inadvertently injected into a blood vessel; these differed from anaphylaxis in the absence of circulatory failure. Similar hallucinatory reactions following orally given probecellin were reported by BJORNBERG (1959).

A serum-sickness-like reaction with fever in a child given benzathine penicillin was described by GOTSIS and HARRIS (1959). A fixed eruption due to penicillin was reported by VERMA (1959). A case of pachymeningitis due to penicillin sensitivity was reported by FARMER *et al.* (1960), and one of erythema multiforme (Stevens-Johnson syndrome) caused by penicillin, in which the body temperature reached 106°F., and which was queried as a case of smallpox, was described by YAFFEE (1959).

KAMDAR (1959) stated that penicillin reactions were to be expected in 2% of children, 5% of non-allergic results and in 15% of allergic adults. In a survey made in Australia of 6,832 patients treated in general practice with penicillin, 88 (1·3%) developed a reaction, 7 of whom had immediate reactions; reactions were less common after oral therapy (*Med. J. Australia*, 1959). In Russia, ASKAROV (1959) compared the side-reactions following 6,200 injections of penicillin and 1,200 injections of streptomycin; the incidence of allergic reactions was 1% and 2%, and of toxic reactions 0·15% and 4·16% respectively.

Penicillin reactions in venereal disease clinics in the U.S.A. were reported by BROWN (1960); of 20,087 patients treated in 1959 the reaction rate was 9·96 per 1,000, whereas of 19,510 patients treated in 1954 it was 5·95 per 1,000. The apparent increase may have been due to a greater awareness and the more recent practice of keeping patients in the clinics for 30 minutes after injection.

The toxic, microbiogenic and allergic reactions to antibiotics were considered by WILLCOX (1959) who found that 57·1% of female and 76·5% of male patients attending a venereal disease clinic in London had had penicillin at some time. Discouragement of the indiscriminate use and abuse of antibiotics except on sound therapeutic and prophylactic indications would lessen reactions to antibiotics of all types. Pictorial examples of advertising pressure on doctors were given.

JOHNSTON and CAZORT (1959) noted that penicillin caused more deaths than any other drug and considered that properly done skin tests would prevent most of these. Reactions are generally allergic, not toxic. On the other hand BACHARACH *et al.* (1959) found penicillin the least toxic of 10 antibiotics tested.

Hidden sources of penicillin in milk, virus vaccines, contaminated syringes, etc., which may cause sensitization, were considered by SIEGEL (1959), and BIRD (1960) urged that penicillin should no longer be added to blood stored for transfusion. EPP (1959) described a new serological procedure for detecting antibodies to penicillin.

The treatment of anaphylaxis was considered by ZUSSMAN (1959), and the use of penicillinase in the treatment of allergic reactions by HURIEZ *et al.* (1959). That penicillinase, which will destroy penicillin *in vivo*, will evoke anti-penicillinase antibodies which destroy the effect of penicillinase was noted by WEISS and CREPEA (1959).

SCIPLE *et al.* (1959) found that the simultaneous administration of an anti-histamine drug did not reduce the incidence of reactions. VANDOW (1959) recommended that subjects sensitive to penicillin should have

20 gm. of a broad spectrum antibiotic in doses of 2–4 gm. daily instead.

(c) *Other reactions.* LARKIN (1959) used nystatin to reduce bacteria overgrowth with thrush in patients treated with tetracycline; he gave 250,000 units of nystatin 4 times daily in addition to tetracycline, and there was no diarrhoea or mouth thrush. On the fifth day 11 of 19 patients treated with tetracycline alone had yeasts in the rectal swab, but only 2 of 18 treated with both antibiotics in combination.

Gonorrhoea

Clinical

Gonorrhoea in the female was considered by BLINICK (1959) and in young girls by BANASZKIEWICZ and GUTAKER (1960). According to GARSON and BARTON (1960) existing methods fail to detect the gonococcus in 25–50% of females. A case of gonococcal arthritis in a girl aged 16 years was recorded by CARNEY (1959) Among 70 women with salpingitis treated with penicillin by HEDBERG (1959) 1 tube was later found by hysterosalpingography to be obstructed in 18 cases and 2 tubes in 14.

Pathological

TAUBER and GARSON (1959) reported the isolation and chemical properties of the lipopolysaccharide phosphoric ester endotoxin from the gonococcus. The mortality of mice infected with Ehrlich ascites tumour cells was shown by TAUBER *et al.* (1959) to increase considerably on injection of sublethal doses of such toxin.

RINGERTZ (1960) described a modified Stuart's transport medium, and STUART (1959) showed that swab specimens could survive in transport medium up to 4 days of transport time. CROOKES and STUART (1959) used aerosporin satisfactorily to inhibit coliforms in gonococcus cultures.

DEACON *et al.* (1959) showed that a species-specific antigen was found in freshly isolated gonococcus cultures and in infectious exudate which could be labelled with fluorescein and used to identify gonococci in smears. Rabbit antiserum to gonococci killed by formalin was coupled to fluorescein isothiocyanate and was shown to react strongly with both cultural gonococci and those in films of urethral exudate. Strong cross reactions with group A and B meningococcus, and to a lesser extent with group C and *Neisseria catarrhalis,* were noted. Adsorption of labelled antiserum with fresh or boiled group A meningococci abolished this cross reaction but left the fluorescence with gonococci in urethral smears unimpaired. It was noted that the fluorescence was well developed when cultures of gonococci 12–16 hours old were tested with the conjugated antiserum, but was less marked when the cultures were 30 hours old. For detection of gonococci in women DEACON *et al.* (1960a) applied the immediate fluorescein staining technique and the delayed staining technique after primary culture, and compared those with cultural procedures. Results of the direct method were inferior to those of culture but by the delayed fluorescein method, results were obtained which were comparable with those obtained by cultivation.

Treatment

(a) *Penicillin.* The development of lessened sensitivity of the gonococcus to penicillin is receiving increasing attention (WHO, 1959; see also BROWN, 1959, and KING, 1960); at the moment it is lessened sensitivity rather than true resistance. As alternative drugs are available, the rapid development of complete clinical resistance is unlikely, though once resistance starts it may proceed at an accelerated rather than at a uniform rate.

GJESSING (1959, 1959a), in Oslo, found increasing failure rates in gonorrhoea treated with 300,000 units of procaine penicillin; rates rose from 2·2–2·6% in the period 1952–1954 to 8·6–11·0% in 1957; the dosage has since been increased. That the dosage should be raised to 600,000–1,200,000 units was the view of KING (1959a). In the U.S.A. GARSON and BARTON (1960) reported a reduction of treatment failures from 15% to 1·7% when the dose was increased to 1·8 mega units of procaine penicillin with aluminium monostearate (PAM), or 600,000 units of this preparation plus 1·2 mega units of benzathine penicillin.

BAKKER *et al.* (1960), from Rotterdam, investigating failures following treatment with 600,000 units of procaine penicillin found some strains which could be grown in the laboratory in the presence of 0·1–0·3 units of penicillin per ml. BARILE *et al.* (1959) had 7 failures in 165 cases in which 600,000 units of procaine penicillin daily for 3 days had been given. The sensitivity of the gonococcus to penicillin ranged from 0·125 to 0·50 unit per ml. of medium. It was considered that repeated low serum levels of penicillin, as produced by prophylactic tablets, etc., was a factor in inducing resistance. The less sensitive strains showed considerable morphological changes. In one case an L form was noted after exposure to penicillin, and this was resistant to high concentrations of the antibiotic. The authors considered it possible that such forms might be induced *in vivo.*

HIRSCH and FINLAND (1960), in the U.S.A., tested the *in vitro* susceptibility of the gonococcus to 20 antibiotics and to sulphadiazine, comparing the results with those of an earlier survey. There was evidence of slightly diminished sensitivity to penicillin at the second survey, but there was no evidence of a serious deterioration. Nevertheless, HIRSCH *et al.* (1960) considered that "a significant adjustment" in dosage schedules was indicated.

Not all suspected penicillin failures are related to the sensitivity of the gonococcus to penicillin. In some the identity of the organism is in doubt, others are due to reinfection even though the possibility of this may be denied by the patient, and others too are due to the failure of penicillin to reach the gonococcus in adequate amounts, from a variety of causes. For example, of two patients with urethritis in which organisms resembling gonococci were found, and which had proved to be penicillin resistant, INO *et al.* (1959) showed the organism to be *Mima polymorpha* var. *oxidans.* LEJMAN (1958), from observations of gonococci, considered that they might retain their viability

for some time after being engulfed by neutrophils. To help in the solution of the many complex problems involved, the recommended creation of a WHO "Gonococcus Centre" as a logical focal point for research was welcomed by McElligott (1960).

Hilton (1959) treated 64 patients with 1·2 mega units of PAM plus 0·5 gm. of Probenecid every 6 hours for 24 hours; 58 patients were followed, and there were no failures, but there were 8 reinfections.

(b) *Other antibiotics.* Durel (1959) proposed the use of two antibiotics (*e.g.*, streptomycin and spiramycin) to combat the development of resistance. Spiramycin was used by David *et al.* (1959); of 19 patients followed after a single dose of 2 gm., 16 were cured. Marmell and Prigot (1959) reported 15 of 16 patients cured when 8 gm. were given over 4 days. The same authors (1959a) also used kanamycin. All of 10 patients were cured with 1 gm. given intramuscularly each day for 3 days, but only 3 out of 10 with a single dose of 1 gm. No untoward reactions were noted and this treatment was considered useful for penicillin-sensitive patients. Schwimmer and Henderson (1959) treated 5 patients with single injections of Synnematin B, which produced a response in all. Although this antibiotic has some structural resemblances to penicillin, and all patients treated were known to be penicillin-sensitive, no signs of allergy were noted. Thomson (1959) used the tetracyclines in a dosage of 1·0 gm. given in 2 doses 8 hours apart plus 0·5 gm. of the long-acting sulphonamide, Lederkyn. In 109 followed there were 8 failures (7·4%).

Willcox (1960a) assessed the effect of steroids in conjunction with tetracycline phosphate. In 32 patients given 750 mgm. of tetracycline alone there were 4 failures, and the same number of failures occurred in 32 others given the same dose of tetracycline plus 12 mgm. of methyl prednisolone. Longhin *et al.* (1959) used cortisone (50 mgm.) followed by corticotrophin plus antibiotics in patients with resistant gonorrhoea, non-gonococcal urethritis, and in females with pelvic inflammatory disease, with satisfactory results.

Ophthalmia neonatorum

Solomons *et al.* (1959) either irrigated the eyes with distilled water, or gave no prophylactic treatment, to 5,480 newborn infants; 76 developed a purulent and 243 a watery ocular discharge. Gonococci were cultured from none although one case was suspicious, and viral or chemical irritants in the mother were suspected as the possible cause. Ropke (1959) considered that prophylaxis could be dispensed with, as ophthalmia is easily treated when it occurs and it may lead to the discovery of gonorrhoea in the mother. However, in view of the resurgence of gonorrhoea, routine prophylaxis has been re-established in a number of places, including the Presbyterian Medical Center, New York (Sprunt, 1959).

Sulphathiazole (20%) was used by Dynenson *et al.* (1959), and sodium sulphacetamide and 1% silver nitrate were compared by Cousineau and Lloyd (1958) on 1,000 newborn; infections of various kinds were lower after silver nitrate but chemical reactions were more marked. Only one case of specific conjunctivitis was reported by Pöschel (1958) in 12,000 infants given penicillin prophylaxis. Bacitracin and silver nitrate were compared by Nelson (1959) who considered bacitracin had a wider range, and by Posner *et al.* (1959) who found gonococcal conjunctivitis in 5 out of 1,935 given sterile water, in 4 of 1,996 given bacitracin with phenocaine ointment, but not in any of 3,165 treated with 1% silver nitrate.

Granuloma Inguinale

Granuloma inguinale was considered by Greenblatt *et al.* (1959, 1959a), and 47 cases of vulvar ulceration in Jamaica due to either granuloma inguinale or to lymphogranuloma venereum by Stewart (1959).

Goldberg (1959) investigated the growth factors of *Donovania granulomatis,* including a low oxygen-reduction potential (satisfied by thioglycollate media), and a factor or factors found in egg which might be substituted by enzymatic digests of bovine albumin and soya meal.

Ghosh and Ghosh (1959) treated a patient with granuloma inguinale by injecting 100 mgm. of erythromycin intramuscularly twice a day for 15 injections. The lesion healed rapidly but penicillin and streptomycin were later given for sinuses in the groin.

Lymphogranuloma Venereum

Lymphogranuloma venereum was discussed by Bedson (1959); and by Greenblatt *et al.* (1959, 1959a). In French Guiana Floch and Mailloux (1959) reported that 4% of 362 healthy persons had a positive Frei (skin) test and 6·5% of 1,037 healthy persons reacted to the complement-fixation test. In Stanleyville, in the Congo, Osterrieth (1959) reported that 18% of hospital patients had a positive complement-fixation test, as did 25% of those suffering from venereal disease. Higher rates were found in patients from the interior.

Jorgensen (1959) studied 8 cases (2 male) in detail at post-mortem. The average age at death was 60 years and the average duration of illness was 26½ years. 7 had rectal stricture and 1 had polyserositis.

Non-Gonococcal Urethritis

Aetiology

A review of non-gonococcal urethritis in Japan, with a detailed study of 162 cases was made by Minekichi Hirakida (1959).

Common bacteria were grown from 8 of 67 subjects with non-gonococcal urethritis by Ujvary *et al.* (1959) and the condition responded to antibiotics after the antibiogram had been determined. Grimble (1959) found pleuropneumonia-like organisms in 9 of 26 patients but also in 11 of 90 unselected males. Complement-fixing antibodies were found in 20% of 118 unselected patients, and of 11 female patients with complement-fixing antibodies 9 were sex partners of males with non-gonococcal urethritis. The evidence that pleuropneumonia-like organisms were the cause

of the condition was considered to be inconclusive, although they might be in some cases.

CSONKA and FURNESS (1960) performed chick-embryo-cell cultures on material from 17 cases of non-gonococcal urethritis and from 3 of Reiter's syndrome for the production of cytopathic effects and inclusions. In only one case (of Reiter's syndrome) were suspicious bodies found but these could not be continuously passaged.

CATTERALL and NICOL (1960) investigated 56 couples with trichomoniasis. CATTERALL (1960) found *T. vaginalis* in 126 of 2,300 subjects with non-gonococcal urethritis (5·5%). The symptoms were usually mild, but 71·4% complained of a discharge. The organism was found by urethral scrapings in 88·8% and by culture in 92%. It was present in 85% of sexual partners.

Treatment

LEACH (1959) had a 73% success rate in 41 patients given 500 mgm. Sigmamycin 4 times daily for 5 days. WILLCOX (1959a) treated 100 patients with 6 gm. of triacetyloleandomycin over 6 days with a re-treatment rate of 27·1% within 3 months. 12 other patients were treated with 4 gm. over 4 days by CSONKA (1959), with 3 failures. JELINEK (1959) had a 75·3–82·5% cure rate with combined streptomycin and sulphadiazine at a cost of 4s. 2d.–6s. 10d. per patient compared with only 61·5% in a 4-day course of tetracycline at a cost of 23s. per patient.

LAIDIG (1959) considered that there was no difference in cure rates between patients treated with antibiotics and those treated symptomatically. ROSEDALE (1959) found that the relapse rate (22·9%) in 83 men whose consorts were also treated was no lower than for men whose consorts were not treated. SIBOULET (1960) considered that more than half of patients with non-gonococcal urethritis required psychotherapy. They soon became anxious and unstable, and frequently showed true anxiety, melancholia and psychic disturbance associated with individual, familial, marital or occupational problems.

If treatment measures remain somewhat unsatisfactory for the common run of cases of non-gonococcal urethritis, a significant advance has occurred in those due to *Trichomonas vaginalis* by the use of metronidazole (Flagyl or 8823 RP). SYLVESTRE *et al.* (1960) used 250 mgm. twice daily for 10 days on 32 cases, with disappearance of the parasite in all. DUREL *et al.* (1960) treated 13 with the same dosage and similar immediate results, although *T. vaginalis* recurred in one case and the discharge persisted without the parasite being found in 3. 11 other males were satisfactorily treated with 200 mgm. 3 times daily for 5 days by NICOL *et al.* (1960).

Reiter's Syndrome

The Fiessinger-Leroy Reiter syndrome was considered by BEERMAN *et al.* (1959), CAMUS (1959), CSONKA (1959a), KESTEL *et al.* (1959), KOZLOWSKI and ZABIELLO (1959), and particularly as regards keratosis blennorrhagica by ALBERT and CRONE (1959), ELLIS and BERESTON (1959) and by SHATIN *et al.* (1960). The surface manifestations, with colour pictures, were presented by HANCOCK (1960) in a review of 76 patients. Balanitis circinata was noted in 26%, lesions of the buccal cavity in 10%, and keratoderma blennorrhagica in 7·8%. Mucocutaneous lesions, especially on the glans penis, were found in 80% of 38 patients by MONTGOMERY *et al.* (1959a).

OATES and CSONKA (1959) described 14 cases in females: only 4 from a total of 213 at one hospital were of that sex. Another case in a female was described by WARNER *et al.* (1960). A case in which the disease developed into classical rheumatoid arthritis was described by LUCHERINI and CECCHI (1958). MASBERNARD (1959) described 80 cases which followed an outbreak of dysentery among French soldiers in Tunisia; urethritis, mostly abacterial, occurred in 80%, eye involvement in 94% and arthritis in 96%.

The radiographic appearances in 25 cases of Reiter's syndrome, 81 of rheumatoid arthritis and 38 of ankylosing spondylitis were studied by MASON *et al.* (1959). In Reiter's syndrome a calcanean spur was characteristic, being found in 20%. Destructive joint lesions were common in the feet but rare in the hands, and sacro-iliitis was noted in 32%. In rheumatoid arthritis the hands were a little more commonly affected than the feet, and sacro-iliitis was found in 12%. In ankylosing spondylitis, sacro-iliitis was present in all cases, arthropathy of the feet in 24%, but of the hands only in 4%. STORSTEIN and WAALER (1959) reported 2 cases of rheumatoid arthritis with aortic insufficiency.

CATTERALL (1960a) investigated 222 patients with uveitis: 142 (64%) had chronic prostatitis, 29 (13%) had ankylosing spondylitis, 14 (6%) developed atypical sacro-iliitis and 7 (3%) had plantar fasciitis. The Rose-Waaler differential sheep agglutination test was positive in only 5%. The complement-fixation reaction for pleuropneumonia-like organisms was positive in only 16% and the gonococcal complement-fixation reaction in 11%. The erythrocyte sedimentation rate was raised in 35%. Uveitis was also considered by CROSS (1959); by the *Amer. J. Ophthalm.* (1959) and by SCHLAEGEL and LEVITT (1959). The Institute of Ophthalmology of Columbia Presbyterian Medical Center in New York will commence a 3-year research project on this condition, which is responsible for 10% of the blindness in the U.S.A. (*Sight Saving Rev.*, 1959). HALLETT *et al.* (1959) noted that the C-reactive protein test was often related to a raised erythrocyte sedimentation rate in uveitis.

OGRYZLO *et al.* (1959) undertook electrophoretic determinations in 8 cases of Reiter's syndrome and noted an increase in alpha 2 and beta fractions. BLOOMFIELD (1960) used the latex-fixation test for rheumatoid arthritis (which is negative in Reiter's syndrome) and found that 15 of 232 syphilitic sera reacted—suggesting that syphilis may produce false positive results in such a test.

Treatment

Views on treatment continue to vary. VANCEA (1959) found penicillin useless but chlortetracycline and phenylbutazone effective. STEINMETZ and GREEN

(1959), describing 16 cases, 8 of which followed gonorrhoea, found penicillin and streptomycin useless but the steroids more effective than salicylates: recovery took 2–5 months. Cortisone was used in Algeria by ROUMAGNAC *et al.* (1958), and in a patient showing the complete triad plus keratosis blennorrhagica, treated by WARNER *et al.* (1960), apparent response to prednisone was noted, although MONTGOMERY *et al.* (1959a) considered that the condition was not influenced by corticosteroids.

Other Conditions

A case of mucocele of the urethra was described by DOYLE (1959), and scrub typhus in the differential diagnosis of venereal disease was considered by LEVY (1959). Two cases of Peyronie's disease (chronic indurative cavernositis) were reported by GHOSH *et al.* (1960) who injected the nodules with 0·25–0·4 ml. of a hydrocortisone suspension twice weekly for 12 injections, claiming good results.

Primary venereal herpes simplex in the male was considered by DUXBURY and LAWRENCE (1959). The virus from a vesicle was isolated in baby mice. The serum of the patient showed a 22-fold increase in neutralizing antibody between the acute phase and convalescence. Two cases of genital cancer, one of the penis arising in pre-existing Bowen's disease, and one of the scrotum in an ex-chimney-sweep, were described by COLLINS (1959).

Mycotic and vaginal infections were considered by CORSTON (1959) and by HESSELTINE (1959), and vaginal thrush by CLARK and SOLOMONS (1959).

Trichomoniasis

Pathology

T. vaginalis was studied under the electron microscope by ANDERSON and BEAMS (1959) and by WELLERSON *et al.* (1959); BAERNSTEIN (1959) undertook metabolic studies. The action of alkaloids upon the parasite was investigated by BODALSKI *et al.* (1958).

The cytology of vaginal smears in patients with *T. vaginalis* was studied by BAUER *et al.* (1959). COMBESCOT *et al.* (1959) noted that for successful experimental vaginal infection in the rat oestrus was required. NEWTON *et al.* (1960) found that germ-free guineapigs were more susceptible to inoculation with *T. vaginalis* than conventional guineapigs. The relation of *T. vaginalis* vaginitis to cervical cancer was studied by KOSS and WOLINSKA (1959).

CLARK and SOLOMONS (1959) considered that diagnosis by culture was more accurate than by wet smear. LAMBOTTE (1959) noted that of 202 specimens 87 were positive by culture and only 38 by direct examination.

Incidence

NETTER (1959) indicated that in France 1 gynaecological patient in 7, and in private practice 1 in 9, have *T. vaginalis*. HOO (1959) found that 14·2% of 1,000 married women in Singapore were infected. LAMBOTTE (1959) noted infection rates in Liège of 17·1% in gynaecological patients, 35·4% in patients with a vaginal discharge and 34·3% in antenatal patients.

Epidemiology

The epidemiology of trichomoniasis was considered by WILLCOX (1960b). There was much evidence to indicate venereal transmission, but in view of the great discrepancy in the numbers of known female and male cases, extravenereal transmission by means of towels and lavatory seats remained also possible. The higher incidence in persons of low socio-economic status, in poor hygienic conditions, would support this.

BURCH *et al.* (1959) demonstrated infection of fomites. White Protestants in Washington, D.C. were more often infected than non-Protestants (Jewish and Roman Catholics). *T. vaginalis* was frequently associated with *T. tenax* in the mouth.

Although some investigators, *e.g.* MCEWEN (1959), regard *T. vaginalis* largely as a symptom arising from vaginal cytological changes produced by hormones as a result of emotional stress, as indicated by MAEDER (1959), it is being regarded more and more as a venereal disease. JIROVEC *et al.* (1959) considered that the parasite was "practically always" transmitted by sexual intercourse.

BLOCK (1959) noted that of 148 male partners 61·5% were infected, and the figures reported by BURCH *et al.* (1959) was nearly 50%, and by WATT and JENNISON (1960) 60% compared with only 8% in 50 controls.

Treatment

A new modified compound of 2–3 dimercaptopropanol (BAL) combined with an arsenical substance (Balarsen) was used locally by BURDINE (1960) and by DE KANTER (1960). Dequallinium was used by LEVINSON (1959) with success in 40% of chronic cases. Tricofuron [furazolidone] and oestrogens, in the belief that trichomoniasis was a manifestation of ovarian dysfunction, were used by HOLTORFF (1959). Pimaricin was reported by CAZEMIAR *et al.* (1959) to be 60–80% effective against *T. vaginalis* and 90% against thrush.

WOTHERSPOON (1960) used hexetidine vaginal gel in 32 cases: in 17 the result was satisfactory, 9 patients were improved, there were 3 failures, 2 had reactions and one was unable to self-medicate. LAMBOTTE (1959) noted that Iturin—an antibiotic from *B. subtilis*—and chlortetracycline would inhibit growth at concentrations of 250 μgm. per ml. and 155 μgm. per ml. respectively, and other antibiotics at various concentrations. A new antibiotic, hydroxymycin, was shown by VAISMAN and HAMELIN (1958) to be effective in mice against *T. vaginalis*. LAMBERT (1959), in a general review, mentioned trials with PA 128, a new antiparasitic drug derived from a species of streptomyces.

The most striking event of the year has been the confirmed success of metronidazole (8823 RP; Flagyl) which is effective orally and has rendered unnecessary the use of the very large number of relatively unsatisfactory local preparations previously available—see DUREL *et al.* (1959).

DUREL *et al.* (1960) treated 6 patients orally and in later work (DUREL *et al.* 1960a) increased the series to 23 with 6 failures. They also used the drug both orally and locally, together. Of 58 patients treated some discomfort in the stomach was noted by 11, including nausea in 4. Two noted dryness in the

mouth and one each diarrhoea and flushing of the face. No changes in blood picture were observed. Urinary excretion was also studied. RODIN *et al.* (1960) treated 82 patients with 200 mgm. 3 times a day for 7 days. 52 were followed for 3 months and there were 9 failures. 11 of 38 male consorts were shown to harbour the parasite. WILLCOX (1960c), using a similar dosage over 5–7 days, had 2 immediate failures and 7 later relapses in 34 followed: there were no side-effects. NICOL *et al.* (1960) on the same daily dosage over 5 days had 17 failures (14%) in 122 patients followed up.

Syphilis

General

A further annual review of the literature on syphilis has been presented by BEERMAN *et al.* (1960). The diagnosis and treatment of syphilis was outlined by THOMAS (1959) and therapy considered by ARIAS (1959) and by DUREL (1960). Syphilis in relation to tattooing was discussed by DAVIS (1960) who stated that there was a higher incidence of positive serum reactions to syphilis in tattooed than in non-tattooed persons.

Treponema pallidum

The relationship of spirochaetes to protozoa and bacteria was considered by VAN THIEL (1959). The ionic requirements (ammonium, lithium, rubidium and cesium) of *T. pallidum* were investigated by DOAK *et al.* (1959) and the action of proguanil hydrochloride on the organism by SINCLAIR (1959). The staining of *T. pallidum* with fountain-pen ink was described by GOLDMAN and SAWYER (1959) who considered that the McArthur microscope was a satisfactory instrument for its examination. VOLOSCEANU *et al.* (1936) stated that 3 Rumanian strains of *T. pallidum* had been maintained in rabbits for 4 years and more.

An account of the source and early work with the cultivable Reiter treponeme has been given by REITER (1960, 1960a); he stated that MULZER and NOTHAAS had found it virulent in 1928. A study of it under the electron microscope was described by BABUDIERI (1958). POWER and PELCZAR (1959) found that both saturated and unsaturated fatty acids were required for its maximum growth. GASTINEL *et al.* (1960) noted that the Reiter treponeme treated by ultrasonic waves would produce immobilisins after repeated intravenous inoculation into animals, whereas virulent *T. pallidum* so treated would not.

Experimental syphilis

A comprehensive histological study of experimental syphilis in the rabbit was presented by LONGHIN *et al.* (1958). Persistence of infection in the treated rabbit was considered by DEL CARPIO (1959). MUSUMECI (1960) used cortisone in experimental rabbit syphilis; with prednisone, even without penicillin, there was a gradual diminution of the size of the syphiloma up to 20 days, *T. pallidum* being found up to 6–8 days. With penicillin plus prednisone, *T. pallidum* disappeared within 6–48 hours from the lesions which healed in 6–10 days. This author also showed that the Herxheimer effect of pyrogenic killed vaccine produced fever in the controls but not in those given prednisone.

Early syphilis

A case of primary syphilis in a man aged 81 was reported by FIUMARA and WHITE (1960). He owned to 4 different contacts in 3 months. A case of superinfection in the primary stage was reported by GARZÓN and FERRARIS (1959). Oral syphilis received consideration from BRADLAW (1958) and a case of transfusion syphilis was presented by PRABHAKAR (1959).

OBEID-RUGGLI (1960) reported that of 107 patients in all stages of syphilis given 3 intramuscular injections each of 600,000 units of procaine penicillin weekly for 8 weeks, none showed a clinical relapse. MONTGOMERY and KNOX (1959) considered other antibiotics in the treatment of syphilis. Bacitracin and subtilin proved relatively ineffective but the tetracyclines (2 gm. daily for 12 days), erythromycin, carbomycin and novobiocin were reported upon favourably. None were as good, however, as penicillin. MONTGOMERY and KNOX (1959a) used erythromycin in 40 cases of early syphilis. In 21 patients given 250 mgm. 4 times a day for 10 days there were 19 successes and 2 failures. SCHWIMMER and HENDERSON (1959) treated one case of secondary syphilis with a total of 3,600,000 units of synnematin B given in 12 injections over 3 days, with apparent response.

OWINSKA and WASILEWSKA (1959) noted that the Jarisch-Herxheimer-Lukasiewicz reaction in 62 of 112 patients with early syphilis was not prevented by corticotrophin.

Latent Syphilis

The prognosis and treatment of late and late latent syphilis were considered by BARNETT (1959); sero-fast cases appeared slightly more prone to progression. High doses of penicillin were recommended for patients with a positive TPI test by RABITO and MARSON (1959). REBOUL and REBOUL (1959) used an initial intensive course of penicillin followed by 4 series in the ensuing year of 4 fortnightly injections each of 2·4 mega units of benzathine penicillin until the patient became seronegative or until a fall in titre was observed.

Late Syphilis

Syphilis of the pancreas was described by CHARIF (1958). 103 cases of syphilitic juxta-articular nodes were reported from China by LI *et al.* (1959). They were usually found approximately 4 years after infection and *T. pallidum* was recovered in one case. A case of gumma of the orbit recurring after excision of the tumour, and subsequently healing with penicillin, was recorded by HEINC (1959).

Venereal diseases in relation to the eye were considered by RANGIAH (1960) and 75 cases of ophthalmic syphilis were reported by NAGESH (1960). An obscure case of tertiary syphilis in a patient with keratoconjunctivitis who died of pneumonia but whose Wassermann reaction was negative in life was described by HEINZ (1959). VAN DER MEIREN *et al.* (1958) examined the eyes of 125 treated syphilitic patients; of a group of 36 with apparent latent syphilis 6 had ophthalmic lesions.

The treatment of 130 patients with late syphilis with penicillin was considered by TAKENOUCHI (1959). THIERS

et al. (1959) used intravenous chlortetracycline and steroids, advocating the use of the latter to prevent Herxheimer reactions.

Cardiovascular Syphilis

Syphilitic aortitis was considered by DAVIS (1959), GODFREY (1959) and by LORENTZ (1960) who described 27 cases.

VAN DER MEIREN *et al.* (1958a) found cardio-aortic lesions in 3 of 50 subjects with late syphilis believed to have been cured. That there was a higher incidence of cardiovascular syphilis in Negroes than in the White race in the United States was again noted by PHILLIPS and BURCH (1959). In 4,568 patients attending a cardiological clinic in Rio de Janeiro (*Rev. Med. Municipal* 1959) the incidence of cardiovascular syphilis was 11%; the lesions consisted of simple aortitis in 58%, 30% were complicated by aortic regurgitation and 12% by aneurysm of the thoracic aorta. LARSEN (1959) noted a relative decrease of syphilis and an increase of atherosclerotic aneurysms between 1914 and 1956. In the latter year the ratio of atherosclerotic to syphilitic aneurysms was 1:0·4.

The decline in incidence of cardiovascular syphilis was also noted by WEBSTER (1960) in a review of its management. The heart condition should first be treated and stabilized followed by 6–10 mega units of penicillin given over 2–3 weeks.

Neurosyphilis

Neurosyphilis was considered by KUTUMBIAH (1959, 1959a) and general paralysis of the insane by HARE (1959). Although the latter condition was thought to be uncommon today STEEL (1960) reported that 18 patients had been admitted to an observation ward in London during 18 months: no treatment had previously been given in 12. A case of neurosyphilis associated with polycythaemia rubra vera was reported by GARRETT (1959). Lightning pains and trigeminal pains due to syphilis were described by SAHU (1959).

A case of optic atrophy in which nerve fibre degeneration was characterized by pearl-string-like swellings was described by WOLTER and LISS (1959). CAMERON (1959) had a case of Adie pupil following ophthalmic herpes; he suggested that Argyll Robertson and Adie pupils might both be due to lesions of the ciliary ganglion, depending on whether the near fibres, the light fibres or the dilator fibres were predominantly affected.

HAHN *et al.* (1959) reviewed 1,086 patients with general paralysis of the insane in several hospitals. Of 148 patients with severe paresis whose work status 5 years after treatment was known, 37% were working compared with 61–82% with milder forms of the condition. BARRON *et al.* (1959) noted that cases of neurosyphilis might continue to deteriorate without evidence of active infection; it was concluded that syphilitic arteritis of the large cerebral vessels, such as the carotid or basilar, might result in impaired cerebral circulation which was not improved by eradication of the infection.

THIERS *et al.* (1959) reported that 0·1 gm. chlortetracycline given intravenously in 3–4 courses each of 30 daily injections plus a 15-day course of prednisone would relieve the painful crises of tabes dorsalis. LOEBEL and HUTCHEON (1959) claimed that a slow intravenous infusion of 0·1% procaine hydrochloride in 5% dextrose would relieve the pain of tabetic crises within 15 minutes and throughout the 3 hours of infusion and for one hour after it.

Cerebrospinal Fluid. Syphilitic changes in the blood and cerebrospinal fluid were considered by BLUMENTHAL and WULKOW (1960). A simple chemical method for the determination of gamma globulin and total protein was described by PAPADOPOULOS *et al.* (1959). BRODELL *et al.* (1959), on the basis of examinations including 39 patients with syphilis, concluded that the transaminase level of the cerebrospinal fluid was not of clinical importance in neurological diseases.

The new diagnostic tests for syphilis employing specific antigens have also been applied to the cerebrospinal fluid. BÖTTCHER and HIPPIUS (1959) found the spirochaetal agglutination test positive in only 34% of cases of neurosyphilis, but there was a wider selection of cases than reported by previous authors. ANDERSON and KENT (1959) examined 98 specimens of cerebrospinal fluid from confirmed neurosyphilis. The treponemal immobilization (TPI) reaction was positive or weakly positive in 65 and the standard tests (*e.g.*, Wassermann reaction) positive in 55. The TPI reaction was positive but the standard test negative in 17; in 11 the reverse was the case. KOSTANT *et al.* (1959) examined the spinal fluid from 49 subjects with neurosyphilis. The treponemal complement-fixation (TPCF) reaction was positive in 91% and the Reiter protein complement-fixation (RPCF) reaction positive in 85%. Standard complement-fixation tests with cardiolipin antigens were positive in 73%: in 12 cases the TPI reaction was negative.

HARRIS *et al.* (1960) used the fluorescent treponemal antibody (FTA) test on 428 specimens of cerebrospinal fluid; no less than 82 were reactive to this test compared with 18 reactive and 8 weakly reactive with the TPI test, 12 with the RPCF test and 16 with a standard test with a cardiolipin antigen.

Congenital Syphilis

The management of syphilis in pregnancy was considered by SLATKIN and NELSON (1959) and by RANGIAH (1959). GUMPESBERGER (1959) reported that of 233 untreated syphilitic mothers 20–70·6% of the offspring had congenital syphilis, the incidence depending on the duration of infection in the mother. Of 1,217 others a small number of syphilitic infants were born to mothers who had been treated with arsenic and bismuth, but none to those who had been given penicillin before or during pregnancy. The new British Adoption Agencies Regulations require that adopted infants have a serum test for syphilis at not less than 6 weeks regardless of the status of the mother's test (*Lancet*, 1959). MULLER (1959) presented the X-ray appearances in a premature infant, which resembled syphilitic osteochondritis resulting from intra-uterine asphyxia.

The pathogenesis of interstitial keratitis was considered by CANALE (1960). PARISH and MITCHELL (1960)

reported a case of congenital syphilis with paroxysmal haemoglobinuria and with aortic incompetence, and ENG (1959) a case of long-standing congenital syphilis in which very weakly positive conventional serum reactions were obtained and only partial immobilization with the TPI test.

Syphilis was thought to be a cause of mental deficiency in only 12 of 1,900 mental defectives seen over a 12-year period by BERG and KIRMAN (1959): 8 of these had congenital syphilis. NORMAN *et al.* (1959) described the post-mortem findings in a case of juvenile syphilis in which penicillin had been given some years previously; although the infection was considered to be arrested a small active lesion was found in the occipital lobe.

Serology of Syphilis

General

The serological diagnosis of syphilis was considered by GARZON and PEPPANDA (1959). A revised *Manual of Serological Tests for Syphilis* was published in 1959 by the U.S. Department of Health, Education and Welfare. KLINE (1959) reported on the 1956–7 Serology Evaluation and Research Assembly in which 38 laboratories participated, performing 18 non-treponemal, 13 treponemal and 7 Reiter protein tests for syphilis.

HEYMANN (1960) and HEYMANN and STEIGER (1960), in an attempt to standardize reporting, urged the introduction of an International Reagin Unit.

Incomplete antibodies in syphilitic sera were considered by SINNECKER (1959). Electrophoretic investigations on syphilitic sera were made by OTTOLENGHI-LODIGIANI and SPAGNOLI (1959), 1959a) and by MUNTEANU and TRANDAFIRESCU (1959) who showed an increase of alpha globulins in 50% of cases of seropositive primary syphilis and of tertiary syphilis, and in 60% of cases of sero-resistant syphilis. Beta globulins were constantly decreased in the primary period and in about half of the cases of secondary syphilis and sero-resistant cases. Gamma globulins were increased in 25% of cases of seropositive primary syphilis and in all cases of secondary and tertiary cases, but only in 30% of sero-resistant cases and in none of cases of cured late syphilis. In active syphilis the protein values returned to normal as a result of therapy. Changes in serum proteins from various (*e.g.* dietetic) causes, might lead to false positive serum reactions to syphilis. BOIRON *et al.* (1958) considered positive serum tests in Africans who tended to show a higher level of serum proteins with a lowering of albumin and an increase of gamma globulin.

Reagin tests

The simplification of complement-fixation tests by using spectrophotometric methods was considered by FRIEDMAN (1960). GUPTA *et al.* (1959) reported on the testing of over 90,000 sera in India; the Wassermann reaction gave the most and the Kahn the fewest positive results and the Meinicke and VDRL showed the closest agreement. SAMANT *et al.* (1960), also in India, used the Kahn, Meinicke and VDRL flocculation tests; the VDRL gave the highest number of positive findings and roughly the same number of false positive readings as the other two. NAGESH and KUTTY (1959) reported on the use of the VDRL and Kahn in 2,000 cases. SEN and RAO (1959) found the VDRL more sensitive than the Meinicke or Kahn. The VDRL flocculation reaction was also considered by CHACKO *et al.* (1959).

Numerous papers refer to new rapid screening tests. The plasmacrit (PCT) test, for which one drop of capillary blood is required and by which a result can be obtained in 8 minutes, was considered by ANDUJAR and MAZUREK (1959) and by HARRIS *et al.* (1959) who on 109 presumably syphilitic sera had 88·1% positive with this test compared with 70·7% with the VDRL test; with 599 non-syphilitic sera 6·7% were positive compared with 1·2% with the VDRL test.

The rapid plasma reagin (RPR) test, which can also give a result in a few minutes, was used by SIMPSON *et al.* (1959); near or complete agreement with the Kolmer cardiolipin complement-fixation test was obtained in 1,672 cases. VAISMAN and HAMELIN (1960) found that this test was in closer agreement with the TPI test than the Wassermann reaction or flocculation tests. PORTNOY and GARSON (1959) and BOSSAK *et al.* (1960) found the test useful even when performed on unheated serum, although slightly less reactive than the plasma test. JOLLY *et al.* (1960) showed that the RPR tests could be done satisfactorily in tubes in which sodium fluoride was used as anticoagulant making possible a double screening programme for syphilis and diabetes.

The sensitivity and specificity of cardiolipin, the purified antigen used instead of animal heart antigens in the VDRL and other tests, was considered by BOLOGA *et al.* (1959). The Third International Reference preparation of cardiolipin was described by KRAG and BENTZON (1959), and the use of a lecithin-free cardiolipin preparation (Cardchol) on leprosy sera by SCHMIDT (1959); it was highly reactive whereas ordinary cardiolipin was only weakly so.

Treponemal tests

GARSON (1959a) indicated that there are now at least 9 tests with treponemal antigens for syphilis, which fall into 3 groups: (1) those using the whole body of virulent treponemes; (2) those using chemical fractions of same; and (3) those using chemical fractions of the Reiter treponeme, of which there are 11 test procedures. These tests include the *Treponema* immobilization (TPI) test (cost 30–100 dollars a test); the *Treponema pallidum* agglutination (TPA) test; the *Treponema pallidum* immune adherence (TPIA) test, the *Treponema pallidum* complement-fixation (TPCF) test (which costs 3 dollars for a dose of antigen); the *Treponema pallidum* methylene blue test; the whole-body complement-fixation test; the Reiter protein complement-fixation (RPCF) test (which costs 2 cents for a test dose of antigen); the *Treponema pallidum* Wassermann (TWR) test; the fluorescent treponemal antibody (FTA) test and the *Treponema pallidum* cryolysis protein test. The order of developing positivity in syphilis is the RPCF, the TPCF, reagin tests, and the TPI test.

SIEFERT (1959) extracted the protein constituent from Nichol's rabbit-adapted *T. pallidum* and by paper

electrophoresis divided it into 5 fractions, 3 of which were serologically active. PILLOT *et al.* (1960) noted that both *T. pallidum* and the Reiter treponemes possessed 3 antigens—a thermolabile protein, a thermostable polysaccharide and a lipoid; consequently a syphilitic serum will react with Reiter antigen and an anti-Reiter serum with *T. pallidum* antigen (cross reaction). Syphilitic sera will react only with the protein fraction of the Reiter treponeme and not with the polysaccharide antigen—see also DE BRUIJN (1959).

Treponema immobilization (TPI) test

The treponema immobilization (TPI) test was considered by PORTELLA and THOMPSON (1959), by FEGELER (1960) and by RAUSCH (1960) who emphasized its value in clarifying suspected false positive reactions to reagin tests. Its specificity was considered by MEYER-ROHN and FROMM (1959) and its reproducibility by BOKKENHEUSER and RICHARDSON (1959) and by FROMM and MEYER-ROHN (1959). Its use in neurosyphilis was considered by CRAPS *et al.* (1959).

The use of portions of bovine eye (aqueous, lens and vitreous) for the basal medium of the TPI test was described by FUCHS and AHRENS (1959) and by FUCHS *et al.* (1960). HENSCHLER-GREIFELT (1959) used deep-frozen infected rabbit's testes satisfactorily for the test after storage at −80°C. for up to 12 months.

NIELSON and METZGER (1959) tested 539 sera, immune to various micro-organisms and viruses, for immobilizing antibody against *T. pallidum* but found none. FROMM and MEYER-ROHN (1959a), in a consideration of the sensitivity of this test, believed it to be the most valuable single test although it had no place in the diagnosis of primary syphilis. KÁROLYI and KIRÁLY (1959) found that in 129 syphilitic patients, mostly treated, 77 were seronegative to reagin test but were positive to the TPI test, 36 were seropositive but were TPI-negative. BERLINGHOFF and VOGEL (1959) reported that after treatment for primary and secondary syphilis the TPI test became negative in three-quarters of the patients, but in late congenital syphilis only in one-eighth. In other forms, apart from early latent syphilis, there was no evidence that the result of the test was influenced by treatment. DIETZ and SCHNEEWEISS (1959) also found that the TPI reaction remained positive in about 20% of otherwise seronegative cases of treated secondary syphilis; the significance of this is unknown and at present such cases should be watched.

MEINICKE and GAGEL (1959) investigated non-specific immobilization, which might occur in some cases; this was traced to the presence of a treponemocidal substance in the media in some samples of calf albumin. SANDERS *et al.* (1960) stated that such results might be due to the presence of antibiotics or drugs in the serum, to physiological abnormalities or to the development of toxic substances in transit, all of which might result in "no valid test". If the euglobulin fraction was removed and reconstituted a valid test might be obtained in approximately 4 out of 5 specimens.

RABITO and MARSON (1959) considered that TPI-positive sera were protective for the treponeme against penicillin and bismuth.

T. pallidum immune adherence (TPIA) test

MILLER *et al.* (1959) prepared a stable antigen from heated virulent *T. pallidum* made into a suspension and preserved with merthiolate [thiomersal]. It was just as specific as the TPI test in cases of early syphilis and gave higher titres in known syphilitic sera. KIRÁLY and PORGANYI (1960) found the results similar to those of the TPI test in false positive sera.

Treponema complement-fixation (TPCF) test

BOSSAK *et al.* (1960a) used the TPCF test with a deoxycholate extract and another—the TPCF-50—claimed to be more specific and more economic of time and reagents; the latter proved less reactive than the TPI test in late syphilis but more reactive in early syphilis.

Reiter protein complement-fixation (RPCF) test

The RPCF test was considered by PAVLATOU *et al.* (1958); BAUER and PINK (1960); and LYNCH and BINDER (1960).

BROWN *et al.* (1960) believed that the test gave similar results to the TPI test in syphilis but according to KJELLANDER *et al.* (1959) it reacted somewhat earlier in primary syphilis while the TPI test remained reactive for longer in late syphilis when, according to SIMPSON *et al.* (1960), the RPCF test may be expected to be negative in more than 50% of cases of long-standing syphilis. ALLINNE and BERANGER (1959) stated that the TPI test was the best of all and the RPCF (Pallignost) was the next best. There was 83·5% of agreement between the latter with the TPI test, but for the Kahn test agreement with the TPI test was only 58·4%.

LYNCH *et al.* (1960) found the RPCF test highly specific. Of 212 vaccinia cases 57 gave some reaction to one or more standard tests. Only one partially positive result was obtained with the RPCF test and this was negative on repeat.

The Kolmer Reiter protein (KRP) test was studied by BROWN and BUNCH (1959). It proved reactive almost as rapidly as the VDRL slide test and maintained its activity for longer. In non-syphilitic sera the results were similar to those of the TPI test.

Fluorescent treponemal antibody (FTA) test

Experiences with the immunofluorescence test, described by COONS in 1942, now applied to the serodiagnosis of syphilis, have been described by BOREL and DUREL (1959) and by CENSUALES and GAROFALO (1959). Its results seem to follow those of the TPI test more closely than those of other tests involving treponemal antigens, it needs less complicated apparatus, anaerobic conditions are not necessary at any stage, and an antigen of killed treponemes is more convenient than a live antigen. More experience, moreover, is required to read the FTA test, and it is possible to express the results of the TPI test in terms of percentage of immobilization.

According to DEACON and FREEMAN (1960) the FTA test is an example of an indirect reaction. It is carried out in two stages: first *Trep. pallidum* from the rabbit is treated with specific unlabelled antiserum (*e.g.* rabbit serum); then, after washing to remove unreacted serum,

goat anti-rabbit-globulin labelled with fluorescein is applied, to detect rabbit antibody. Treponemes from infected rabbits are placed on a microscope slide, dried, fixed with acetone and then exposed to the human sera to be tested. After washing with saline, anti-human-globulin labelled with fluorescein (the indicator) is added. The technique was also described by OLANSKY *et al.* (1960). Both authors considered that the antibodies detected were the same or similar to TPI antibodies, and the latter—if further experience bears out these claims—that the FTA test might one day replace the TPI test. A modification of the FTA test, with serum diluted 1:200, was described by DEACON *et al.* (1960).

Other treponemal tests

VAISMAN and HAMELIN (1959a, b) used a new *in vivo* test devised by TANI *et al.* (1955) in which a suspension of *T. pallidum* was mixed with the serum to be tested and injected intraperitoneally into guineapigs. Samples were withdrawn after 4 and 7 hours and the treponemes were counted. With negative sera the treponemal count remained constant but with positive sera the treponemes had disappeared at 4 hours, which was confirmed at 7 hours. On 106 sera the results were similar to those of the TPI test. Saline suspensions of organisms (which must be present in large numbers) can be used. No survival media are required.

Treponematoses

The treponematoses as a world problem were considered by GUTHE (1960). Although a big recession in all of the treponematoses has occurred in the last decade, in some countries venereal syphilis has recently begun to increase again and difficulties are being encountered in the eradication of yaws in spite of initial successes. An evolutionary cycle of the treponematoses was proposed by WILLCOX (1960d) who considered the means of transmission of endemic syphilis (bejel, njovera, etc.) yaws, and pinta and showed how extrinsic and intrinsic (within the host) environmental factors influenced the production of particular disease syndromes. The various treponematoses, particularly yaws, were considered in a monograph published in Malaya by TURNER (1959).

Yaws in Venezuela was considered by MEDINA (1959) and in Mozambique by PRATES (1958). There was an estimated incidence of 4% of the 6 million population of Mozambique: in some provinces 25% of patients admitted to hospital suffer from yaws. The anti-yaws campaign initiated in 1952 was now taking effect. Details of the yaws campaign in the Netherlands New Guinea where there were 5% of active and 2·9% of infectious cases were given by KRANENDONK (1958). In Haiti (WHO 1960) where the prevalence in 1950 was estimated at 36·5% it was believed in June 1959 that there would be no more infectious yaws by the end of the year. However, with receding yaws there is the danger of the introduction of venereal syphilis (WHO 1959a; HACKETT 1959). One suggested approach to the new problem is through routine serum tests on expectant mothers.

ENGELHARDT (1959) considered the possible congenital transmission of yaws, which had previously been considered unlikely; he believed that it was not infrequent. DUNLOP (1960) studied 128 coloured immigrants in London with positive serum tests; in 47 there was evidence of past yaws, in 26 of syphilis, 10 patients had had both diseases, and in 45 there was no evidence either way. 6 cases of pinta in Bengal in 1956 and 5 more in 1957 were described by GHOSH and GHOSH (1959a).

Venereal Disease Control

General

Erich HOFFMANN, who with SCHAUDINN discovered *T. pallidum* in 1905, died of a heart attack on 13 May 1959 at the age of 92 (SCHREUS 1959). Venereal disease control was considered by CLARK (1960) and syphilis morbidity by LANDES (1959).

The report of the activities of the International Union against the Venereal Diseases and Treponematoses has been published (*Brit. J. Venereal Dis.* 1960; CLARK and VAN HYNING 1960), its opportunities were reviewed (ACTON, 1960) and its scope in relation to the World Health Organization considered by GUTHE (1960a). The WHO Expert Committee on Venereal Infections and Treponematoses has presented its fifth report, which covers all aspects of control, and this has been published (WHO 1959b). While the present prevalence of infectious syphilis remains at a low level (5% or less of the 1945–7 figures) in many countries there has recently been a significant increase. Gonorrhoea never declined as markedly (to 35–50% of 1945–7 figures) and in recent years increases in gonorrhoea have been widespread throughout the world (GUTHE, 1960).

Africa

Venereal disease in Eygpt were considered by RAGAB (1959). In Tunisia LADJIMI (1960) reported 540 cases of primary and secondary syphilis in 1948, 93 in 1954 and 283 in 1958.

Americas

The role of the facilitator (who assists a person (who may have venereal disease) to meet a healthy person) in the spread of venereal disease in Vancouver, British Columbia, was studied by LARSEN and CUNNINGHAM (1960).

In the United States BROWN (1959a) indicated that there were 4,000 known deaths a year from syphilis; the annual cost of maintaining syphilitic blind persons was 12 million dollars, and of syphilitic insane persons 48 million dollars. Of persons requiring treatment 1 in 200 will become blind, 1 in 50 insane, 1 in 25 crippled or incapacitated to some degree, and 1 in 15 a victim of syphilitic heart disease. Marked increases in gonorrhoea were reported by SINGER and PASTERNACK (1959) in Arizona and by ASHLEY (1959) in Maine. According to the *Report of the Department of Health, Puerto Rico* (1956–7) there was a fall in syphilis but an increase in gonorrhoea. In Michigan, HEUSTIS (1959) reported that it was now possible to receive a certificate for marriage immediately after treatment for early syphilis: formerly one year of satisfactory observation was required.

In New York in the first 6 months of 1959 early syphilis was up 35·9% and gonorrhoea up 14·2% (*New York Med.* 1960). In the U.S.A. as a whole the first increase in syphilis since 1947 was reported in 1956; a further increase occurred in 1957.

In Mexico 9·2% of expectant mothers were seropositive in 1947 but a record low figure of 1·6% was obtained in 1954 (LOZANO, 1960). The venereal disease programme there was discussed by BUSTILLOS MENDEZ (1960).

Europe

Belgian Legislation on Venereal Diseases, 1791–1958, was outlined by CRAPS (1959a); the VD programme in Bulgaria was reviewed by POPCHRISTOV (1960). In Czechoslovakia HEGYI and HUDAKOVA (1960) reported that syphilis was effectively reduced and no marked drives were necessary. A good service had not had such a marked effect on gonorrhoea in areas with a large migratory population. Of 882 persons from a parish register of 974 on the island of Bornholm, Denmark, tested by DENCKER and NIELSON (1959), 14 were seropositive to conventional tests, 16 to the TPI tests; both tests were positive only in 5.

In France LÉPINE (1959) reported an increase of syphilis in the last two years—see also THIERS (1959) and LAUZIER and LAFAGE (1959). In Hungary FÖLDVÁRI and KÁROLYI (1960) reported a fall in syphilis from 15,061 cases in 1947 to 126 in 1954 and to only 5 in the first 9 months of 1959. In Italy COFFARI (1960) reported 17,001 cases of primary and secondary syphilis in 1947, 2,264 in 1954 and 4,345 in 1955, but there had been a new method of notification. The provisional figure for 1958 was 4,375. REALMUTO and CENSUALES (1959) found a 1·4% seropositive among blood donors in Rome.

ENG (1959a) in Norway reported a fall of seropositivity rates in expectant mothers from 0·63% in 1953 to 0·34% in 1958. BRANDAO (1960) reported a striking fall of contagious syphilis in Portugal where, according to CARDIA and DA FONSECA (1960) the prevalence of gonorrhoea was also declining in the gynaecological clinics. According to BOLOGA and JONESCO (1959) syphilis was likewise declining in Rumania. The trends of syphilis in Spain were considered by CUESTA ALMONACID *et al.* (1959) and the laws in that country have been outlined (*Internat. Digest Health Legis.*, 1959).

In the United Kingdom early syphilis continued to fall from 747 in 1957 to 704 in 1958 (but has since risen). Gonorrhoea, on the other hand, has shown a sharp rise from 24,381 in 1957 to 27,887 in 1958 (*Brit. J. Venereal Dis.*, 1959). Between 1951 and 1957 there was over a 50% increase in women (*Med. Officer*, 1959). Venereal diseases in the U.S.S.R. were considered by BEILIN (1960).

Far East

The anti-venereal disease campaign in Ceylon, where the prevalence of syphilis has been reduced and that of gonorrhoea remains much the same, has been reviewed (WHO 1958; 1960a) and venereal diseases in Madura, India, were considered by AYYANGAR (1959). In New Delhi TAMPI and RAO (1959) stated that the non-prostitute promiscuous women were now a more important source of infection than the prostitutes. NIYOGI *et al.* (1959) in Baroda, India, found 3·5% of expectant mothers positive to the Kahn test.

Venereal diseases in the Philippines were considered by VALDES (1959). In Singapore, RAM (1960) reported that there were 3,589 cases of primary and secondary syphilis in 1949, 5,088 in 1955 and 5,233 in 1958. In Tahiti, BORIES and LAIGRET (1959) reported a 4·9–7·0% seropositivity rate to reagin tests in different age-groups.

Case finding

The value of the venereal disease investigator was stressed by ALLISON (1960) and of the public health nurse by CLARKE (1959). The cost of routine serum testing of hospital in-patients as a case-finding tool in Alberta, Canada, was assessed by BELL (1959). Of 13,372 tests only 1·06% were positive. Reactive results were found in 106 patients but in only 4 did this lead to successful treatment, at a cost of $1600 per case. This was, however, considered worth-while for, in addition to syphilis, collagen diseases, such as disseminated lupus erythematosus, might be revealed by proved false positive results. Compulsory free pre-marital and pre-employment serological examinations for state employees and immigrants were recommended by DE FONSECA (1960).

In Michigan, U.S.A., HEUSTIS (1959a) estimated that a new case of venereal disease occurred every hour during 1958 and surveys indicated that 5–10 times as much gonorrhoea was being treated by private practitioners as was being reported; in such circumstances contact tracing was less intensive. The private physician, according to ROGERS (1959) can do little epidemiological work other than treat the patient's spouse. BROWN *et al.* (1959a) estimated that if proper contact tracing had been done on the 12,028 cases notified by private practitioners 2,474 more cases of early syphilis would have been found.

In Dayton, Ohio, WILLIAMS and DOWD (1960) stated that private physicians saw 1,260 patients with venereal diseases compared with 1,434 seen in the clinics. LENTZ (1960) stated of another area that private physicians reported 1,814 cases of syphilis in 1959 compared with only 195 in 1958. LUGAR (1959) stated that one patient referred from a private physician led to the discovery of 12 with early syphilis. Venereal diseases in private practice were also considered by MONTGOMERY *et al.* (1959).

HASSARD (1959) considered privileged communications in relation to venereal diseases, expressing the opinion that professional secrets may be revealed for just causes, *i.e.*, the common good, if grave injury is likely to arise to a third party, if grave harm is likely to arise to the patient if the secret is kept, or if grave harm is likely to occur to the physician.

Problem groups

Migrants. Migration as a venereal disease factor in the U.S.A. was considered in some detail by BROWN (1960a), the health of seafarers by WHO (1959c) and the treatment of venereal diseases in seafarers by ROSE (1959). During the year the World Health Organization, who

administer the Brussels Agreement, have defined standards of diagnosis and treatment for the venereal disease clinics of the world in which seamen are treated. NICOL *et al.* (1960a) presented a social study of 296 coloured patients in London who had admitted 380 sexual contacts within 3 months, 56% of which were with coloured and 44% with white persons.

Homosexuals. Homosexuality in the spread of early syphilis was considered by TRICE *et al.* (1960). LÉPINE (1959) reported an increase of infections in pederasts in France. NICOL (1960) also reported a rising incidence of male homosexual patients in venereal disease clinics in London.

Prostitutes. DUCREY (1960, 1960a) noted an increase in venereal disease in Italy since the brothels were closed but felt that this arose from relaxation of medical examination of prostitutes and notification of venereal diseases *per se*. KEIGHLEY (1960) found that of 2,382 female prisoners in Holloway prison 31 had syphilis, 215 had gonorrhoea and 778 had other conditions requiring treatment: 36% were under 20 years of age, of whom 130 had gonorrhoea.

GARNIER (1959) rejected preventive treatment of prostitutes on grounds of risk of allergy and of masked infections. The psychological aspects of the prostituant were considered by GIBBENS and SILBERMAN (1960).

Teen-agers. A number of epidemics of gonorrhoea among teen-agers have been described (USPHS, 1960). LOEB (1960) has indicated that in the near future teen-ager populations in the large urban cities of the U.S.A. are likely to be increased. The road to promiscuity was considered by O'HARE (1960).

Health Education. Psychological and educational factors in the prophylaxis of venereal diseases were considered by PAGNOZZI (1959). Some discussions with patients with venereal disease regarding their attitude towards those diseases and to sex generally were recorded on tape by DALZELL-WARD *et al.* (1960). CROMWELL (1959) emphasized the value of the school nurse in reaching teen-agers.

FOOTNOTE

The majority of the papers listed, or abstracts of them were published during 1960 in this *Bulletin*, the *Tropical Diseases Bulletin, Abstracts of World Medicine* or the *British Journal of Venereal Diseases*. The author is also indebted to the U.S. Department of Health, Education and Welfare for their annotated bibliography *Current Literature on Venereal Diseases* and to the World Health Organization for references.

Where papers are by two authors, the name of each author is listed in the text: where three or more authors have collaborated, the name of the first with the term *et al.* is used, but the names of all authors are given in the list of references.

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Public Health

The order in this section is:—**General; Vital Statistics; Epidemiology; Maternal and Child Health; Health of Students, Nurses and Hospital Staffs; Health of Old Persons and the Chronically Ill; Chronic Cardio-Respiratory Diseases; Chronic Rheumatism; Cancer; Miscellaneous Diseases; Dental Health; Mental Health.**

GENERAL

ROYAL SOC. PROMOTION HEALTH J. 1960, July–Aug., Sept.–Oct. & Nov.–Dec., v. 80, Nos. 4, 5 & 6. **Health Congress at Torquay, April 25–29, 1960.**

The congress held in Torquay in April 1960 followed the lines of previous congresses; there were many sections, each with its own programme and speakers, and each with its own discussions. The President was Sir John COCKCROFT, who spoke on radiation hazards and precautions, a subject which attracted a lot of attention.

In the section which, in the published account of the congress, follows that on radiation the speakers discussed world population trends and the related health problems, particularly the controllable infections and under-nutrition, and this was followed by the series of papers on food poisoning and its investigation which, though primarily orientated to Britain, have universal application. A related section referred to comparison between British and American standards of food hygiene, and was complimentary to American practice. Hospital sanitation, which includes drainage and ventilation, was treated by an architect well aware of the problems.

The Executive Council's services section concerned itself with general practice and with maternity services, and there was a paper on municipal finance and housing. Mental disorder and the provision made for dealing with it were discussed, with emphasis on occupational therapy in Hull.

In the Occupational Health section there were comments on the contributions which industrial medicine has made to the understanding of many socially important problems, and on the growing enlightenment of industrial leaders. Health visiting received general appraisal in the relevant section.

In the veterinary section the brucellosis problem was summarized and a look was taken ahead at meat factories of the future and the dehydration of meat. The public health inspectors discussed clean air and river pollution. The health education section papers related to the problem of venereal disease in young people, and the engineers discussed heating and housing.

The food and nutrition section took bread, meat and vegetables for its subjects, and the medical officers of health looked forward with some confidence to the disappearance of tuberculosis.

The congress evidently followed the pattern of former years in presenting an informed conspectus of modern opinion on the varied subjects with which it dealt; it is an important record. *Charles Wilcocks*

MCKEOWN, T. **Priorities in Preventive Medicine.** *New England J. of Med.* 1961, Mar. 23, v. 264, No. 12, 594–9, 3 figs.

This is the Cutter Lecture delivered at Harvard in 1960, by the Professor of Social Medicine in the University of Birmingham, England.

There are three sections: Mortality, Morbidity and Services.

Mortality. A diagram compares the female mortality per 1,000 conceptions in 1950–52 with 1838–54: the trend of mortality for males is similar. For the earlier period the abortion rate was assumed to be 200 per 1,000 conceptions and the stillbirth rate 50: for 1950–52 abortions were assumed to be 150 and the stillbirth rate was 21. Another diagram divides the mortality for these two periods into age-groupings; prenatal and neonatal, pre-reproductive, reproductive and post-reproductive. There was little difference over the span of a century in the prenatal and neonatal age-group but a marked reduction in the pre-reproductive and a substantial one in the reproductive group. There was a heavy increase in the post-reproductive age-group. It is concluded—in agreement with the views of HALDANE—that the high mortality during the 19th century in the pre-reproductive and reproductive groups was determined by an unfavourable environment (including infectious diseases) rather than by undesirable genes. "With few exceptions, it is only on deaths before and immediately after birth that one can say confidently that the post-natal environment has had no effect." "Prenatal mortality is largely attributable to the uterus which . . . is the most dangerous environment to which the offspring is exposed between conception and death." In the future most deaths will occur either before birth or after reproduction is completed.

Morbidity. There is a paucity of statistical data but some figures for Birmingham hospitals are given. In the pre-reproductive age-group there is relatively small demand for hospital care: more is needed in the reproductive group (15–44) mainly because of accidents, infections and mental illness: there is insufficient knowledge to enable us to do much preventive work in the mental diseases. The post-reproductive group occupy two-thirds of the hospital beds for females and most are in hospitals for mental or chronic diseases.

Services. The evolution of the medical services has led to a preventive service administered and staffed separately from the curative services but there was no real divorce so long as attention was fixed primarily on infectious diseases. Later, the welfare of mothers and of pre-school and school children was added to the responsibilities of local authorities and all were separated administratively from the curative services which were largely, until 1948, financed privately. Now, when the curative services are publicly financed in Britain, the division between preventive and curative medicine as

thus developed still remains and the author suggests that the proper alignment of the preventive personal services is with curative medicine. The dividing line should now have on one side all types of personal medical care and on the other the environmental services which could be entrusted to non-medical staff provided medical consultants were available and used.

Allen Daley

WORLD HEALTH ORGANIZATION. TECHNICAL REPORT SER. No. 215. **Planning of Public Health Services. Fourth Report of the Expert Committee on Public Health Administration. Geneva. 1–6 August, 1960.** 48 pp. [Refs. in footnotes.] 1961, Geneva: Palais des Nations. [Sales agent for U.K., H.M. Stationery Office.] [3s. 6d.; $0.60; Sw.fr. 2.–.]

This WHO expert Committee on public health administration met under the chairmanship of Sir John CHARLES. The *rapporteur* was Dr. Ira V. HISCOCK of Yale and the other members came from Nigeria, India, Switzerland, Egypt and the U.S.S.R.

In many countries, now well developed, the health services have grown without deliberate long-term planning, and additions have been made from time to time because of urgent needs such as large-scale epidemics. But when there is little or no background of established organization it is essential to have a survey made of the territory and the people so as to obtain information about the state of health of the inhabitants and the services to be developed from existing services, or established anew, for health promotion and protection; the arrangements for training medical and health personnel; what equipment and supplies are needed; and the available financial resources.

The next step after the survey is to settle priorities, and after emphasizing prevention as an essential, to decide on the groups to be selected for early attention, *e.g.* those engaged in productive work or vulnerable groups such as mothers and children. Improvement in nutritional standards may need a high priority.

Broad targets may then be set up. They may include the provision of a health service available free of cost to the entire community or limited to specified groups; a plan to control, or even to eradicate, the most prevalent of the communicable diseases; a community water supply and sewerage. The time set for the attainment of the targets may be 5–15 years and for every target a detailed programme must be devised.

It is essential that all planning be done in consultation with those who will have responsibility for providing the service such as organizations of doctors and nurses; and also with representatives of those for whom they are provided namely the users. It is helpful to have a central research council.

Operational studies on such things as work loads for professional staff and the use made of hospitals and clinics can be of great value.

When the targets and priorities have been settled it is necessary to allocate responsibility for implementation to the different regional, local or individual organizations. On them must be placed the task of planning the details within the money available and of making plans for the trained staff to be available when required.

All these local plans are then assembled centrally and co-ordinated into a final national plan which is now ready for submission to the financial and legislative bodies.

All is not finished when legislative approval is obtained. There must be constant appraisement to ensure that the plan keeps abreast with such things as population changes, medical discoveries, new industrial hazards, and the opening up of new areas by roads or railways. An annual report is a valuable means of assessing progress.

The report ends with a list of topics for future study and emphasizes the value of pilot schemes in the planning of public health services at different levels of governmental administration.

There are 4 appendices. The first is a list of what a public health programme might include: the second gives an outline of the public health planning as practised in six countries: Ceylon, Czechoslovakia, India, the United Arab Republic, the U.S.S.R. and the United Kingdom. The third is very short and just lists possible sources of finance for health services while the fourth is bibliographical and supplementary to the numerous references given in footnotes in the text.

Allen Daley

MANUWA, S. **The Principles and Methodology of Planning the Development of National Health Programmes in Underdeveloped Countries.** *West African Med. J.* 1961, Apr., v. 10, No. 2, 69–86. [15 refs.]

Release of the resources of an underdeveloped country from "the tangled undergrowth of mass disease" is a prerequisite or development. Medical and health services, therefore, must feature prominently in all general schemes of development, for economic reasons as much as those of humanity: health planning must be regarded as part of a combined operation aiming at integrated and balanced development of the national economy. Resources of funds and manpower are usually limited. Health services demand not only a capital outlay but also recurrent funds for their upkeep and adequate trained staff and training facilities. A development plan must recognize these facts, make the maximum use of what is available and provide for the creation of increased resources of materials and human skill. The plan must ensure as far as possible an even nation-wide distribution of benefits; it should aim at orderly progress over a long period, and with limited means available it must be selective—in face of inevitable clamorous demands by local interests.

Planning may be approached in several ways. One method is the appointment of a National Economic Health Planning Commission incorporating a health planning division; or the latter may be a permanent branch of the Ministry of Health. Planning is centralized thus in totalitarian countries, and the system has

produced excellent results. It offers obvious advantages, but is difficult to apply in countries consisting of federated states. Nevertheless, India has central planning control. Within the framework of a broad economic policy laid down by a National Economic Planning Commission and approved by the Union Parliament, a Health Division (on which all States are represented) lays down in broad outline a 15-year health programme, divided into more detailed 5-year and annual segments, for the whole country. The States (Constitutionally virtually autonomous in health affairs) work out the further details of their requirements within this framework, and are then allocated grants for the implementation of approved health proposals by the Commission. This system provides for partial decentralization, with a measure of central control through the budgetary mechanism. Both are desirable, since local planners are in intimate touch with their area, but disease is international and local efforts must be co-ordinated.

For a major review of a country's health services, a special Commission may be appointed. This may consist of one man, but more commonly of several. The composite Commission possibly works more slowly but should produce more comprehensive results. Its work should not be hurried. The Bhore Commission in India took 26 months to complete its report. In selecting the members of such a Commission, it must be remembered that the recommendations of distinguished foreigners on unpopular subjects are always more likely to be accepted than those of prophets in their own country, and to attract international aid. But local knowledge must be strongly represented, to fill gaps in written records and prevent ill-informed criticism of existing institutions, and unrealistic proposals. The Commission should be free to call on the advice of outside experts and, especially if its members are of local origin, to visit other countries with similar problems. The terms of reference must be broad, but must include a comprehensive review of the present state of the country's health problems and existing services, assessment of needs and resources, and recommendations for development—both immediate and long-term. The Commission may have to arrange for sample surveys, where the pattern of disease is not accurately known.

Chief priorities in an underdeveloped country would be: the preventive services (prevention being better and cheaper than cure); environmental sanitation; endemic and epidemic diseases, particularly those most readily controlled by mass campaigns; provision of services to productive workers, specially in agriculture (though industry is becoming of increasing importance); health of the vulnerable groups; recruitment and training of all types of health staff; improvement of nutritional standards and of the collection and processing of vital statistics. It is specially important to recognize that the success of a plan depends greatly on the confidence and co-operation of all sections of the community.

High priority should be given to polyvalent mobile field units, which undertake campaigns, curative and prophylactic, against mass diseases, and also collect valuable statistics. They are the "panzer corps" of medical services, not an end in themselves but a means to an end—the permanent establishment of rural health—in which static services carry out the "mopping up" operations.

In the Federation of Nigeria [of which Sir Samuel Manuwa was Chief Medical Adviser] there is no Constitutional provision for federal grants for specific regional development projects. The Indian system may be difficult to apply, but there seems to be no reason why a National Health Council, comprising Federal and Regional representatives, should not be established. If public health planning is to remain dynamic as it becomes increasingly complex, there must be the highest attainable degree of co-ordination. It has been suggested that the time has come to rid the hospital services of bureaucratic control, by handing over their control to autonomous unofficial bodies. The principle is sound, but it must be remembered that in the United Kingdom this system developed on a long-established basis of voluntary service; it would be dangerous to introduce it in an underdeveloped country without careful consideration.

The exiguousness of medical services makes it imperative to place greater emphasis on preventive rather than curative services. "However, whatever the relative emphasis may be, the fact remains . . . that the economy of this country ultimately depends on the good health of its teeming agricultural population . . . and the preservation and maintenance of its health must be our first care." *B. B. Waddy*

WORLD HEALTH ORGANIZATION. TECHNICAL REPORT SER. NO. 216. **Recommended Requirements for Schools of Public Health. Tenth Report of the Expert Committee on Professional and Technical Education of Medical and Auxiliary Personnel. Geneva, 12–16 December 1960.** 24 pp. 1961. Geneva: Palais des Nations. [Sales agent for U.K., H.M. Stationery Office.] [1s. 9d.; $0.30; Sw.fr. 1.–.]

The chairman of this WHO expert committee was Dr. E. L. STEBBINS of Johns Hopkins University; the vice-chairman Dr. V. V. ERMAKOV of Moscow and the *rapporteur* Dr. N. JUNGALWALLA of New Delhi. The other members came from France, Australia, Egypt, Chile and England (Professor W. S. WALTON). The objective was to agree upon standards which would be suitable minima for schools of public health. As a preparation for the meeting a questionnaire had been sent to 50 schools in 32 countries and in 44 it had been completed and returned.

The definition of a school of public health which was adopted was "an institution with adequate resources which, in addition to research in public health and service to the community, provides a full-time course lasting not less than one academic year, or its equivalent, covering the subjects essential to the understanding of the various problems of public health and the concepts, organization and techniques required for dealing with them, and which is open to members of the medical and allied professions seeking qualifications in public health".

The main function of a school is to give specialist

training to those medically qualified but there are advantages in admitting to suitable parts of the courses those without a medical background. There are short paragraphs on the part that schools of public health could play in the training of public health engineers, public health nurses, dentists and veterinarians who are to work in the public health field, health statisticians, hospital administrators and teachers of preventive and social medicine in undergraduate medical schools. It is strongly urged "that a school of public health which does not carry out research does not meet its obligations". A school should always be prepared to serve the community in whatever way is opportune.

There are about 60 schools of public health in the world. The 41 which have provided statistics contain almost 2,500 students. The annual intake ranges from 6 to over 100: the optimum number is thought to be 30–50 and if it is consistently over 50, consideration should be given to the provision of an additional school. From the world point of view the numbers of both schools and students are inadequate for the needs.

Each school should be organized into at least 5 departments (1) public health administration: principles and practice; (2) health statistics; (3) epidemiology (4) environment health; and (5) microbiology. Details are given of what should be included in each department.

The teaching of public health practice may be entrusted to full-time academic or to part-time staff whose main work is the administration of the local health services, but in the latter case more junior full-time academically qualified staff should also be employed. The teacher: student ratio needs to be high, such as one full-time staff member, or equivalent, to 3 students.

A school should have, by arrangement with the responsible organ of government, its own training area where the staff is provided by faculty members of the school or jointly appointed by the school and the health authority. In one country the training includes provision for practical work by "residency" (registrar) appointments and the report says that this development is "noted with interest".

In discussing the contents of the curriculum it is stated that, as it has to be confined to one year, it should concentrate on basic training in public health though it is desirable to allow some scope for "elective" subjects in which individual students are specially interested.

The average amount of time occupied by various forms of teaching were found to be: lectures, 45%; discussions, seminars and visits, 20%; laboratory work, 21%; and field work, 14%.

A section sets out methods of training other than by a one-year full-time course. They include specialization in public health during the undergraduate medical course; a course of 3 months full-time in each of 3 years; a 2-day-a-week course for 2 years; correspondence courses lasting for 8 to 24 months together with 2 separate courses each of a month and full-time at the teaching institution; 1-year courses of special study leading to a doctorate in public health and available only for those who have already taken the basic 1-year full-time course. *Allen Daley*

VITAL STATISTICS

ENTERLINE, P. E. **Causes of Death responsible for Recent Increases in Sex Mortality Differentials in the United States.** *Milbank Memorial Fund Quarterly*. 1961, Apr.; v. 39, No. 2, 312–28, 4 figs. [Refs. in footnotes.]

Male mortality in the United States, in common with other western countries, is larger than the female mortality and the ratio of male to female death rates has steadily increased during the present century. The largest rise in the mortality sex ratio has been at ages 15–24, owing to the increase in motor-vehicle deaths among males and to the fall in the death rate from other causes for both sexes. The rise in the ratio at ages 45–64 has been due to the rising trend of the male death rates from lung cancer, motor-vehicle accidents and coronary heart disease and to a decrease in the death rates from causes that chiefly affect females: maternal mortality, cancer of the uterus, tuberculosis, etc.

The author suggests that environmental factors may be important in the age-groups where the mortality sex ratio has increased the most. *W. J. Martin*

WORLD HEALTH ORGANIZATION. TECHNICAL REPORT SER. No. 218. **Expert Committee on Health Statistics. Seventh Report. Geneva, 5–10 December 1960.** 28 pp. 1961. Geneva: Palais des Nations. [Sales agent for U.K., H.M. Stationery Office.] [1s. 9d.; $0.30; Sw.fr. 1.–.]

MATERNAL AND CHILD HEALTH

LONDON COUNTY COUNCIL. **Report on the Heights and Weights (and other Measurements) of School Pupils in the County of London in 1959** [SCOTT, J. A., Principal School Medical Officer]. 63 pp., 5 figs. [22 refs.] No. 4086. 1961. London: The County Hall, Westminster Bridge, S.E.1. [1s.]

The school health service of the London County Council began to compile the heights and weights of school children in 1904. From 1935 until the outbreak of war a 6-monthly record was made for every school-child. It was resumed in certain parts of the county in 1942 and restored fully in 1948. In 1952 it was restricted to the 4 routine medical inspections and discontinued altogether in 1959.

From time to time the results were analysed fully and published. The last previous survey was for the year 1954 and it was felt that it was getting out of date. For the 1959 survey, representatives of the government departments concerned and of the Institute of Child Health were invited to assist in the planning. To avoid random error, over 20,000 children had to be included and the schools selected were chosen so as to give due weight to social class, religion and type of secondary education. Sufficient children were included in each of the 9 divisions into which the county is divided to enable comparisons to be made between the divisions. The measurements were made by the same two specially briefed health visitors in each division. The numbers measured were 25,568 covering an age range of 4 to 16. The children were weighed in pants and vests only, the weight of which was known, and the figures given are the nude weights. Calf and upper arm circumferences were measured with a steel tape and measurements of skin-folds made with Harpenden calipers. The older children were asked supplementary questions about the onset of puberty as shown by a break in the voice or when menstruation began, and about the size of the family. The data were transferred to punched cards which were counted and sorted mechanically.

The results are set out in 22 tables and 8 diagrams. In brief, both boys and girls are taller than in the survey of 1949: at age 5 the increase is about 0·5 cm.; at age 6, just over 1 cm.; and at age 10, 1·5 cm.; thereafter except for girls aged 14 and 15 they were about 3 cm. taller. There is an indication that girls are attaining adult stature at about the age of 16.

Weights also are increasing though the increases were smaller between 1954 and 1959 than they had been between 1949 and 1954. Over the 10 years from 1949 the gain for both sexes was about 0·3 kgm. at age 5 rising to about 1·5 kgm. at 10 and 3 kgm. at 11 to 12. After this age the increase among the boys was 4 to 5 kgm. at 13 to 14 declining to 3·5 at 15, whereas for girls the maximum was 3·5 kgm. at 13 declining to 0·8 at 15. These increases in the average weight have come about not so much by a general uplift as by a disproportionate increase in the number of heavy children.

The differences in the measurements of children in different parts of the county have continued to lessen. A table in the text shows that as age advances from 5 to 16 years there is an increase in the weight per centimetre of height, and at all ages there has been an increase in weight for any given height.

Comparisons of the 6 measurements taken show a close relationship between height, weight and each of the 2 circumference measurements. There was a fairly high correlation between the 2 circumferences and the skin-fold measurements but little between these measurements and height.

The spurt in growth associated with puberty took place in girls about 2 years earlier than in boys but when it did come in boys it was bigger. The criteria used to give the onset of puberty were not very exact, specially for boys, but they show that in 1959 the mean age at which 50% of the boys had reached sexual maturity was 13·83 years (14·15 in 1954) and for the girls 13·05 (13·29 in 1954).

The answers to the question on family size indicated a constant pattern of lower height and smaller weight as family size increases. An unexpected finding is that the girls, but not the boys, in large families tend to mature late. There has been some slackening of the increases of height and weight at the lower ages in the last quinquennium and it may be that the absolute increase in growth is coming to an end and that any future increase will be due to earlier puberty.

Allen Daley

CARTER, F. S. **Paediatrics in Freetown, Sierra Leone.** *Arch. Dis. in Childhood.* 1961, Apr., v. 36, No. 186, 190–99. [24 refs.]

Practising for 4 years from October 1955 to September 1959 as physician at the main hospital in Freetown, the capital town of Sierra Leone, the author was in exclusive control of the chilren's ward during his last 6 months there. This enabled him to make a detailed analysis of the case histories of 422 infants and children under 11 years of age—the total admissions in March–September 1959.

There was a mortality rate of 25%. Of 102 who died, 27 did so less than 6 hours after admission, 60 in the first 24 hours, and all but 17 within the first week. These rates are similar to those described by MACGREGOR in Ibadan [this *Bulletin*, 1959, v. 34, 2]. The highest mortality was in the youngest infants (44% at 0–6 months; 37% at 6–12 months). Moribund children were frequently brought to hospital so that a medical certificate of death could be obtained for the Registrar of Deaths.

The diseases diagnosed, and mortality from each disease are listed in a table. The main diseases or groups of diseases were: pneumonia, bronchitis and bronchiectasis (84); *P. falciparum* malaria (70); kwashiorkor and marasmus (64), measles (40); dysenteries (29); typhoid fever (2); whooping cough (29); tuberculosis (29); tetanus neonatorum (23), tetanus of childhood

(4); coryza and tonsillitis (20); sickle-cell crises (9), various other diseases (68). Out of 143 consecutive haemoglobin estimations made on admission, 104 (72·7%) showed haemoglobin levels of 70% or less.

All children except neonatal infants were Mantoux tested on admission, and 222 tests (excluding deaths and discharges) were read; of the 26 children with positive reactions and 3 with false positive reactions, 20 were found to have tuberculous lesions. Calcified hilar glands were not uncommon and fibrocaseous disease of the adult type was seen, the general pattern of tuberculosis approximating to that seen in England. This contrasts with Carter's experience in Nairobi [*ibid.*, 1954, v. 29, 1038].

Nutritional diseases were by far the most important group in the ward. Malnourished children might be in hospital for several weeks or more, and minor degrees of malnutrition were an underlying factor in many other of the diseases treated. A few 60 ml. bottles of serum albumin (equivalent to the albumin in 1 pint of blood) were available, and one bottle was given intraperitoneally to kwashiorkor patients by the method described by Carter in an earlier paper (*E. African Med. J.*, 1953, v. 30, 499). During the second day there was frequently a marked diuresis with a reduction in oedema. Though of undoubted therapeutic value this therapy was limited by expense.

Intraperitoneal transfusions of blood were also given with success. Carter has found this technique to be preferable to intravenous transfusions, which in West African conditions requires unremitting personal supervision.

He concludes that much childhood mortality is due to parental ignorance, fear, and superstition leading to fatal delay in hospital treatment. Mortality will not be reduced until education in public health measures becomes effective.

[This is an interesting account of hospital paediatric practice, and there are personal observations of clinical differences seen by Carter in Freetown and Kenya. The large number of admissions of moribund children, and the reference to death certificates show clearly that this hospital population was highly selected. Death certificates were not a legal requirement for local people in Freetown, but the Registrar required some information about deaths for the medical officer of health. This information was often supplied by chemists, who in their shops probably conducted, with inadequate medical training, the bulk of general medical practice in the town (except traditional "native medicine"). There was therefore a tendency for their failures to appear in hospital—often as "penicillin failed".

The ready availability of non-protein plasma substitutes for transfusion may conceal the need for a well organized local supply of real plasma and blood. Carter describes his personal ingenuity in obtaining blood for transfusion, and many enterprising medical practitioners make similar personal arrangements, but these makeshifts only emphasize a basic lack in hospital facilities which costs many lives.] *T. P. Eddy*

HEALTH OF STUDENTS, NURSES AND HOSPITAL STAFFS

QUEEN'S UNIVERSITY OF BELFAST. **Student Health Committee. Report of Medical Officer** [JOHNSTON, W.]. **Twelfth Annual Report. Academic Year 1959–60.** 7 mimeographed pp. + 21 pp. of tables. [1961.]

The twelfth Annual Report of the work of the Student Health Service of the Queen's University of Belfast in the academic year 1959–60 records a lower general morbidity rate than in previous years. Upper respiratory infections were less in evidence than is usual in winter and there was no influenza epidemic.

The medical officer draws attention to the marked increase in cases of psychoneurosis with a larger number of students than previously requiring specialist psychiatric advice: 4 students had to be treated in hospital for prolonged periods. Johnston is of the opinion that the majority of those suffering from psychoneurosis would have done so in any walk of life but in a few the illness was probably precipitated by the strain of present-day university life. More students than ever are dependent on grants, and failure in an examination may lead to withdrawal of the grant and the end of the student's university career.

The results of the routine examination by the visiting mass radiography unit are given in detail. Once again there were no defaulters. 3,227 students were X-rayed and active pulmonary tuberculosis was found in 3 (0·9 per 1,000); all were males. 1 student who was under supervision because of inactive pulmonary tuberculosis developed tuberculosis of the wrist during the year. Johnston believes that the present favourable situation is entirely due to the annual X-ray examination with consequent early detection of the disease and immediate segregation and treatment of the patient. He has found no evidence at any time that the infection originated or was transmitted within the university. He adds "Tuberculosis is, however, a disease which is always with us and any relaxation of the present regime would, I am quite sure, have quite disastrous result".

The number of students vaccinated with BCG at school increases yearly. All continue to have annual tuberculin tests and information is being collected which will show how long tuberculin sensitivity following vaccination persists in young adults in Northern Ireland. *H. G. Calwell*

CHRONIC CARDIO-RESPIRATORY DISEASES

ACHESON, R. M. & THORNTON, E. H. **Mortality from Coronary Artery Disease and "Myocardial Degeneration" in the Republic of Ireland.** *Brit. J. Preventive & Social Med.* 1958, Apr., v. 12, No. 2, 82–93, 7 figs. [23 refs.]

"(1) Comparative mortality indices show that, for every death in a man or a woman in the Republic of Ireland certified as due to angina pectoris in 1926, over thirty deaths were certified as being due to angina pectoris or coronary artery disease in 1956.

"(2) The secular rate of increase in the male and female death rates has been approximately equal and uniform.

"(3) Comparative mortality indices for the group of diseases which are now classed as myocardial degeneration show little change for the period 1926–1956 for either sex.

"(4) The groups of the population which have borne the brunt of the secular increase in deaths certified as due to coronary artery disease are men in early middle age and old age, and women in old age.

"(5) Coronary artery disease is more frequently certified as a cause of death in the boroughs of Cork, Dublin, and Dun Laoghaire than in any rural area; the incidence of deaths attributed to this cause is much higher in rural areas to the east of the Republic than those to the west.

"(6) The importance of coronary artery disease as a certified cause of death as compared with all other causes of death has increased greatly in the past 30 years; again, in men the greatest increase is in early middle age and old age, and in women in the older age groups.

"(7) The death rate due to coronary artery disease in the Republic of Ireland in 1954 was lower than that in many of the countries whose statistics for that year have been published by the World Health Organization; the average mortality rates for both sexes aged 45–64 in Dublin City and Dun Laoghaire from 1951–1955 were much lower than those in rural *or* urban areas of England and Wales in 1950–1952.

"(8) As the incidence of deaths due to coronary artery disease has increased, so the male/female sex ratio in the various age groups has changed, and the greatest changes have been among the younger age groups in whom certification is likely to be less erroneous. It is suggested that the relationship observed in the Republic between overall incidence of deaths due to coronary artery disease and the sex ratio for the various age groups may be a universal phenomenon."

ACHESON, R. M. **Mortality from Cerebrovascular Accidents and Hypertension in the Republic of Ireland.** *Brit. J. Preventive & Social Med.* 1960, July, v. 14, No. 3, 139–47, 4 figs. [10 refs.]

This paper is complementary to a similar study [see above] on coronary artery disease. Mortality data from cerebrovascular accidents could be analysed over the 3 decades from 1926 to 1957. Owing, however, to changes in the method of diagnostic classification the analysis of deaths from hypertension was confined to the years 1950–1956.

The crude Irish death rate from hypertension showed little secular change after 1950. There was a slight increase in the crude death rate for cerebrovascular accidents between 1926 and 1949 (from 0·9 to 1·3 per 1,000) and a rather more rapid increase between 1950 and 1956 (from 1·3 to 1·8 per 1,000). The rise over the whole period is chiefly accounted for by an increased rate in both sexes at the oldest ages. The rates among women under 54 have shown a fall over the same period, explicable by the fall in the prevalence of rheumatic heart disease and in the consequent risk of embolism. The incidence of cerebrovascular deaths in each sex shows in each decade a steady upward trend with age. Both cerebrovascular and hypertensive deaths are commoner at all ages in women than in men. The male-female ratio increases with age in cerebrovascular disease and approaches unity at the oldest ages, but shows little age change in hypertension.

Within Ireland itself there is no well defined geographical pattern in cerebrovascular mortality, only a suggestion that the rates are higher in town than in country and in the south-east than in the north-west. The range of variation is higher in females than in males, and the highest female rate is some 3½ times that of the lowest rate. Age-standardized death rates from this disease and from hypertension and from coronary disease were calculated for each sex for a number of countries including Ireland for the year 1955. The male rates were highly correlated with the female rates, in these different countries as well as in the different Irish counties, for each of the 3 disease groups. Between the 3 pairs of diseases, particularly high correlations were obtained, both intra- and internationally, in the case of coronary disease and hypertension. Cerebrovascular accidents were strongly correlated with each of the other 2 disease groups in the counties of Ireland in the case of males, but not in the case of females. In the different countries the corresponding correlations were insignificant and mostly negative.

In the discussion of the results the shortcomings of the data are stressed. For instance, cerebral embolism and cerebral thrombosis are quite distinct aetiologically but are grouped together in the latest international classification. Hypertension may be the cause of death, yet it may be absent in the terminal stages and thus overlooked by the medical attendant. Alternatively it may be listed as only a contributory cause and so escape classification. The author concludes generally that different standards of diagnosis and the proportion of deaths occurring in hospital must contribute largely to the inter- and intra-national differences and to the secular trend in the recorded death rates.

[The data and the discussion, in this rather unpromising field, are presented with clarity and judgment.

The author comments: "Few facts of epidemiological value have resulted from this analysis. It does, however, illustrate admirably the pressing need (stated by WHO, 1959) for a thorough scientific study of the methods whereby vital statistics are collected all over the world."] *A. S. Fairbairn*

See also p. 861, PAUL, **Chronic Bronchitis in African Miners and Non-Miners in Northern Rhodesia.**

CANCER

BALLENGER, J. J. **Experimental Effect of Cigarette Smoke on Human Respiratory Cilia.** *New England J. of Med.* 1960, Oct. 27, v. 263, No. 17, 832–5, 3 figs. [24 refs.]

The effect of cigarette smoke on the ciliary activity of human respiratory epithelial cells was examined *in vitro*. The subjects of the experiment were children 3–10 years of age. A cup 2–3 mm. wide was passed through the glottis under vinyl ether anaesthetic and the superficial layers of epithelium scraped off by 3 or 4 separate strokes. The specimen was transferred to a special salt solution and stored for several hours. Minute bits of epithelium were then placed in clot containing chick embryo extract and chicken plasma on a coverslip and examined in an air-tight and water-tight well of a glass slide. The cilia can normally be seen to beat for 2–3 weeks. Aggregates of cells detach and form irregular masses with the cilia outwards and these masses are caused to rotate by the beating of the cilia.

When the clot was bathed in the special salt solution the rotation continued for 36 to 48 hours. When the fluid was replaced by a solution which had been exposed to the smoke from 2 mechanically smoked cigarettes rotation stopped within 5 to 28 minutes and the rotating body later disintegrated.

It is suggested that cigarette smoke may have the same paralytic effect on the cilia *in vivo*. This would result in a prolonged contact between the cigarette tars and the bronchial mucosa, which might be important in relation to carcinogenesis.

[It is unfortunate that the author does not explain why the children from whom the specimens were obtained were anaesthetized. Presumably this was in the course of a necessary medical procedure, but in the absence of an explanation some readers may question the propriety of the investigation.] *Richard Doll*

See also p. 869, HATEM, **[Mechanism of Cancer Induction by Metals. Role of Histamine and Prophylaxis by EDTA].**

MISCELLANEOUS DISEASES

RAMALINGASWAMI, V., SUBRAMANIAN, T. A. V. & DEO, M. G. **The Aetiology of Himalayan Endemic Goitre.** *Lancet.* 1961, Apr. 15, 791–4, 5 figs. [22 refs.]

The investigation described here was undertaken to study some aspects of iodine metabolism mainly in children living in the extensive Himalayan goitre belt which stretches from Kashmir in the west to Bengal and Assam in the east.

The children under study were of 3 groups—(1) from an area of goitre prevalence of 50% to 60%—15 boys and 18 girls ages 12–16, (2) from an area 600 miles from the first area of goitre prevalence of nearly 100%—30 boys and 13 girls ages 8–12, and (3) from a control area free of endemic goitre about 150 miles from the second area—9 boys and 9 girls aged between 12 and 15 years. Some adults from the endemic areas were also included and studied in comparison with adults in Delhi, which is non-endemic.

The investigations included measurement of the radioactive iodine (^{131}I) uptake by the thyroid and determination of the serum-protein-bound iodine (PBI). Methods are described with the results which are set out in tables and figures.

"The results showed increased avidity of the thyroid for iodine in endemic goitre associated with low serum –PBI levels. The results are consistent with the view that the Himalayan endemic in the two areas is probably causally related to an environmental iodide deficiency. They also show that the deficiency is extreme."

There is a discussion in which reference is made to the finding of low PBI values in some goitrous children being at variance with the findings of values within normal limits in reported studies of endemic areas in other countries. *M. E. Delafield*

MENTAL HEALTH

LAMBO, T. A. **The Influence of Cultural Factors on Epidemiological Surveys in Africa.** *West African Med. J.* 1961, Apr., v. 10, No. 2, 87–92.

In several of his recent papers [this *Bulletin*, 1961, v. 36, 12, 427] the author has stressed the importance of cultural environment, and community tradition, on the incidence and the outcome of mental disorder in Africans. He amplifies this conception, in general terms, in the present paper—a lucid and convincing exposition of an obviously important point of view—and he extends the conception to include the effect of attitudes of mind on the course of physical disease.

He makes the important point that the tolerance of abnormality is less permissible in a stratified and highly sophisticated culture than in a more primitive society where the family unit is larger and more tolerant. He writes from Western Nigeria, where religious ceremonies are largely concerned with prevention of disease, and where the Africans retain traditional beliefs in the causation of disease which tend to make them sceptical of some European methods of treatment.

In view of this he has made use of "the so-called African witch doctors", and has in this way been able to obtain "invaluable data on the nature and clinical measurements of certain diseases". He notes that growing urbanization of Africans and the new economic order tend "to eliminate the role of the elderly members of the society", and he implies a growing social cause of mental distress.

[This is a far-sighted approach to an obviously difficult and serious problem. The old society had the virtues of stability, but is no longer in the inevitable modern stream of social evolution.]

Charles Wilcocks

Sanitation

The order in this section is:—**General; Water and Swimming Baths; Sewage, Trade Waste and Refuse Disposal; Housing; Infestation; Atmospheric Pollution; Port, Ship and Aviation Hygiene.**

WATER AND SWIMMING BATHS

(Including the Bacteriology of Water Supplies)

DEPT. SCIENT. & INDUST. RES. **Water Pollution Research 1960. The Report of the Water Pollution Research Board** [GARNER, F. H., Chairman] **with the Report of the Director of the Water Pollution Research Laboratory** [SOUTHGATE, B. A.]. pp. vi + 122, 57 figs. & 4 pls. [Refs. in footnotes.] 1961. London: H.M. Stationery Office. [7s.]

In this the 28th Annual Report of the Water Pollution Research Board there is mention of the coming into force in 1960 of the Clean Rivers Act which brings under the control of River Boards new discharges into most of the estuaries of England and Wales. Also a section of the Research Laboratory is to be transferred early in 1961 to premises made available at East Kilbride to enable the Laboratory to keep in closer touch with industry, local authorities and River Purification Boards in Scotland. Arrangements are also being made by the Organization for European Economic Cooperation for a first meeting of representatives of the principal countries in 1961 which is to be attended by the Assistant Director of the Laboratory.

The Report of the Director of the Water Pollution Research Laboratory gives a clear picture of the wide scope of the researches initiated or continued during 1960.

Researches on the basic processes for the treatment of polluting liquids included studies on comparison of media of different types and size for use in percolating filters; aeration in the activated sludge process by diffused-air systems and mechanical aerators and sedimentation phenomena in humus tanks.

Much valuable work was done on industrial waste waters which included investigations on the dewatering of sludge from calico printing; the biological treatment of coke oven effluents; the treatment of waste waters containing cyanide and of other wastes from farms, meat-processing, a fellmongery, the manufacture of rag felt and chipboard and from aircraft cleaning.

The section on sewage contains a report on the examination of the flow and composition of storm waters at Brighouse, Bradford and Northampton which is being carried out for the Ministry of Housing and Local Government. In addition there are descriptions of work on the nature and concentration of organic constituents of sewage effluents and sludges; the dewatering of sludge and the use of a radioactive tracer to study mixing in an anaerobic digester. There is also an account of the progress of the large-scale trials in Luton of the new anionic surface-active material (sodium Dobane JN sulphonate) which were previously described in the Reports for 1958 and 1959 [this *Bulletin*, 1960, v. 35, 1082]. Other research described in the sewage section was on the clarification of effluents by chemical

coagulation and on the removal of nitrogen from sewage during treatment by the activated-sludge process and by biological filtration.

The effects of pollution on fish continue to receive very much attention. The work on the influence of suspended solids on fish begun last year has been continued in the laboratory and by a survey of streams polluted with wastes from the china-clay industry. Experiments have been made on the toxicity of gas liquors, of metals, of a proprietary "filming amine" and of orthophenylphenol.

Fresh-water streams were investigated to study aeration at weirs, oxygen consumption and algal and other plant growths. The results of a survey of the amounts of radioactive strontium passing down the River Thames are reported. This survey made at the request of the Ministry of Housing and Local Government showed that "The levels of activity observed in samples of river water were very low indeed, and the mean concentrations calculated over periods of about 14 weeks were in all cases well below the maximum permissible levels".

The final report on the Survey of the Thames Estuary cannot yet be completed owing to its detailed nature, the complexities of the subject and the further experimental work that has been found to be necessary from time to time but it is hoped that 11 out of a total of 18 chapters of the final draft will be completed by the end of the year.

The final section on "Instruments and Methods" contains an account of new devices and the investigation of methods. The items in this section are automatic sampler; recording the rotation of distributors; polarographic measurement of dissolved oxygen; recorder for suspended solids in sewage effluents; sludge detector; determination of organic carbon; determinations of oxidized nitrogen; radiochemical analysis of samples of water, aquatic vegetation and mud; the determination of specific resistance to filtration, and the use of lithium for measurement of rate of flow.

There are appendices on publications during 1960, membership of committees and senior staff of the Research Laboratory. *M. E. Delafield*

World Health Organization. **European Standards for Drinking-Water.** 52 pp. [61 refs.] 1961. Geneva: Palais des Nations. [Sales agent for U.K., H.M. Stationery Office.] [3s. 6d.; $0.60; Sw.fr. 2.–.]

A few countries in the European Region of the World Health Organization have succeeded in establishing standards of quality applicable to their respective territories and in achieving a certain degree of uniformity in the expression of results and methods of analysis. The Regional Office for Europe of WHO has been conducting a study in collaboration with member governments and, with the assistance of a number of experts, has now published this document concerning the quality of drinking water in Europe. The report is concerned with the minimal chemical and bacteriological quality that might reasonably be expected of piped supplies of water for domestic use.

The report first deals with bacteriological examination and, after defining the organisms indicative of pollution, it sets out recommended methods for their detection and estimation together with standards of quality to be expected in piped supplies of drinking water. Correct sampling procedure for bacteriological examination is emphasized and there is special reference to the frequency of sampling in the distribution system. The latter is an important and necessary branch in waterworks control because pollution may happen in the distribution system as in the waterworks.

Physical and chemical examination includes methods of examination and limits of toxic substances, including radioactivity. A second group of chemical substances to which limits are applied are those which may give rise to trouble in piped supplies but not necessarily amounting to ill health. A third group includes substances of which the level should preferably be controlled, such as ammonia, free carbon dioxide, dissolved oxygen and total hardness. The fourth category consists of general examination of the water for its physical, chemical and aesthetic characteristics.

Among the appendices are specimen forms suggested for reporting the results of bacteriological and chemical examination of water.

It should be stressed that the proposals set out in the report are intended only for the guidance of health officers, analysts and others whose duty it is to provide a safe and attractive drinking water; they are recommendations and in no sense mandatory.

E. Windle Taylor

Gärtner, H. & Schyma, D. Uber den Nachweis von Coli-Bakterien und Salmonellen aus dem Wasser mit einem löslichen Ultrafilter. **[Estimation of *Escherichia coli* and Salmonella from Water by means of a Soluble-Ultrafilter]** *Arch. f. Hyg. u. Bakt.* 1961, Mar., v. 145, No. 2, 81–7.

In former publications the authors [this *Bulletin*, 1960, v. 35, 1080, 1164] described the structure of one of the soluble ultrafilters developed for the concentration of micro-organisms from water samples. The filter consists of a water-rich gel of aluminium alginate 0·5 mm. thick which is soluble in a very small quantity of 3·8% sodium citrate solution. In the present work the aluminium alginate filter is compared with other methods. Results from plate counts, membrane filtration and alginate filtration were compared on water samples of known bacterial content. It was shown that the quantitative recovery of both *Escherichia coli* and salmonellae from water samples was possible by filtration through aluminium alginate. The authors claim that a combination of filtration through alginate and tetrathionate enrichment gives an improved method for the detection of pathogenic intestinal organisms in heavily polluted waters. The great advantage of the alginate filters lies in the possibility of collecting large numbers of bacteria and differentiating them both quantitatively and qualitatively.

E. Windle Taylor

DAUBNER, I. Ein Beitrag zur Frage der Nitratreduktion durch Bakterien der Unterfamilie Escherichieae. **[Nitrate Reduction by Escherichieae]** *Arch. f. Hyg. u. Bakt.* 1961, May, v. 145, No. 3, 196–200, 1 fig. [10 refs.]

This paper contains the results of a study of nitrate reduction by bacteria in which it is well known that substances such as ammonia and hydroxylamine may be the end result of the reduction and not nitrite.

560 strains of 5 different members of the sub-family Escherichieae were isolated from surface waters, drinking water and human faeces and examined in the nitrate reduction test over a period of 5 days at 37°C. Qualitative tests for nitrite were carried out at 3, 5, 8, 12, 24, 48, 72, 96 and 120 hours. These tests were positive in 194 strains at the end of 3 hours and in only 233 strains at 120 hours but at 8 hours all the 560 strains gave a positive result. At 12 hours' incubation there were 7 negatives after which the number of these increased progressively to the maximum.

It is suggested that in the nitrate reduction test the examination for nitrite should be made after 8 hours of incubation. *M. E. Delafield*

BUCZOWSKA, Zofia & NOWICKA, Barbara. **Locating *Salmonella* Infection Sources of River and Bathing Beach by means of Sewage Examination.** *Bull. Inst. Marine Med. Gdańsk.* 1960, v. 11, Nos. 3/4, 139–46, 1 fig.

This is an account of investigations at the Baltic coastal town of Orlowo (population 12,000), which includes a newly-built area with adequate sewerage and an outfall discharging sewage effluent after sedimentation into the local river, together with an old town south of this with cesspools whose effluents overflow into storm-water channnels and thence into the river. Sporadic cases of typhoid fever occur in the town every year. During the period of the present study, *viz.* April to December 1959, 4 isolated cases occurred, 3 due to phage type J_1 and 1 to type D_1. One of the type J_1 cases was probably infected by a known typhoid carrier. The source of infection of the other 3 patients was not detected. One of the 3, a permanent resident boy of 14, is stated to have bathed frequently, and in the conclusions the statement is made that the remaining 2, who were holiday visitors, " could have been infected when bathing," although this is not mentioned in the body of the paper.

A comprehensive attempt was made to investigate the topographical distribution of samonellae, including the typhoid bacillus, in the sewers and in the river and the sea, by using the sewer swab technique for sewage samples and filtration of water samples through diatomaceous earth or membrane filters, with selenite enrichment and plating to Wilson and Blair medium. Of 397 sewer swabs, 77 yielded salmonellae on culture, and 11 of these *Salmonella typhi.* Sewer swabs gave more positives than direct culture of sewage samples, and selenite enrichment was far more fruitful than direct plating. The sewer swab survey gave some indication of the parts of the town from which typhoid bacilli were being discharged into the sewers, but, partly because of inadequate access to individual house drains, no typhoid carrier was detected.

Salmonellae, including *Salm. typhi* of phage types D_1, F_1 and J_1, and also *typhi-murium, enteritidis, paratyphi B,* Give and Newington, were isolated from samples of river water and from the sea water of the bathing beach.

[This is a bacteriologically competent study, but a total lack of critical information makes it quite valueless in assessing the possible health risks of sea bathing.]

B. Moore

v. WASIELEWSKI, E., CARLSON, S., HUSMANN, K. H. & CHRISTOFORIDIS, G. Modellversuche zur Überlebensdauer pathogener Viren im Rheinwasser. **[The Survival Time of Pathogenic Viruses in Water of the Rhine]** *Arch. f. Hyg. u. Bakt.* 1961, May, v. 145, No. 3, 184–9. [27 refs.]

A short account is given of the relatively few papers which have been published on the epidemiological importance of human pathogenic viruses in river water and on the inactivation of such viruses in a river.

In the study here described the Rhine, which is polluted from many sources, was chosen for the experiments. The river water was examined by a number of chemical tests and by a microbiological investigation, the results of which are recorded.

Below Mainz the water is considerably more polluted than it is above the city. Samples of 1,000 ml. of water from the Rhine above and below Mainz and also of the filtered and heat-sterilized river water were inoculated with suspensions of either Theiler or encephalomyocarditis (EMC) viruses from the brains of mice which had recently died from these virus infections. These inoculated water samples were shielded from the light and were continuously agitated. The rate at which the viruses were inactivated was assessed by determining the LD50 in white mice of the subcutaneous or intracerebral injection of small volumes of the infected water at intervals ranging from 5 to 264 hours.

The main finding which is discussed was that the rate of inactivation was directly related to the degree of pollution of the water, being greatest in the water from below Mainz and least in the filtered, sterilized water.

M. E. Delafield

SEWAGE, TRADE WASTE AND REFUSE DISPOSAL

SCHULLER, A. J. Bestimmung des biologischen Sauerstoffbedarts im Warburg-Gerät im Vergleich mit den herkömmlichen Methoden BSB_5 und dem Kaliumpermanganatverbrauch. **[Determination of the Biochemical Oxygen Demand by the Warburg Apparatus]** *Arch. f. Hyg. u. Bakt.* 1961, May, v. 145, No. 3, 201–14, 10 figs. [38 refs.]

This paper contains a full account of a large number of experiments on 36 samples of sewage and 6 of surface waters which were examined by the Warburg respirometer in order to study the suitability of this method for determining the biochemical oxygen demand by comparison of the results with those obtained with the standard 5-day biochemical oxygen demand (BOD) method and the oxygen absorbed from permanganate.

The results of these experiments—set out fully in tables—were analysed statistically in comparison with each other and are discussed.

The main conclusion of the author is that the Warburg apparatus is of value in that the oxygen uptake can be observed continuously and that it is possible to calculate from the amount of oxygen absorbed in the first 8 hours the amount that will be absorbed in 24 hours. No precise relation of the Warburg figures with the 5-day BOD values could be established although the Warburg 24-hour at 25°C. oxygen absorbed figure amounted to about 55% of the 5-day BOD.

M. E. Delafield

ATMOSPHERIC POLLUTION

MARTIN, A. E. **Epidemiological Studies of Atmospheric Pollution. A Review of British Methodology.** *Monthly Bull. Ministry of Health & Pub. Health Lab. Service (directed by Med. Res. Council).* 1961, Mar., v. 20, 42–9. [15 refs.]

HECHTER, H. H. & GOLDSMITH, J. R. **Air Pollution and Daily Mortality.** *Amer. J. Med. Sci.* 1961, May, v. 241, No. 5, 581–8, 3 figs. [30 refs.]

Reviewing recent studies of acute and chronic effects of air pollution the authors discuss inherent difficulties of studies in this field. Ranking high among such difficulties are those of interpreting results obtained from time series correlations of the seasonal phenomena involved. Again, the lack of an easily measurable and sensitive biological indicator is a serious limitation to ascertaining effects from low level pollution. Mortality, while easily measured and thus commonly used, is far from sensitive.

The paper presents some further analyses of the environment (temperature oxidant and carbon monoxide concentration) and mortality (cardiac and respiratory deaths) data of Los Angeles County for the years 1956 to 1958. In correlating the factors under study the seasonal component of each series was isolated and removed by the techniques of harmonic analysis and further adjustment was made for associations between successive daily observations. None of the partial correlations remaining between mortality and pollution factors were statistically significant, and this negative result was taken as indicating that changes in the daily air pollution level, as measured by oxidant and carbon monoxide concentration, exerted no detectable influence upon the day-to-day mortality patterns. It is emphasized, however, that these findings, dealing only with the acute terminal response of man to variations in air pollution, do not lessen the importance of air pollution as a possible menace to the health and well-being of man.

J. T. Boyd

ARCH. ENVIRONMENT. HEALTH. Chicago. 1961, May, v. 2, No. 5, 544–74. **Air Pollution Control.**

The meeting to which these papers were presented was devoted to 2 topics. In the morning the subject was "Air Pollution in a Typical Eastern City" and in the afternoon it was "Automotive Exhausts: Pollution and Control".

The essentially local interest of the meetings is indicated by the fact that the typical Eastern City is not Singapore or even Moscow but Philadelphia.

The titles of the individual papers are:—

Philadelphia's Air and Sources of Pollution by R. SMITH (pp. 545–8); *Meteorology and Topography of Philadelphia Region* by F. DAVIS (pp. 549–53); *Local Health and Nuisance Aspects* by Katherine R. BOUCOT (pp. 554–6); *The Automotive Exhaust Problem* by D. HOFREUTER (pp. 559–63); *Automotive Exhaust Control Problems* by W. L. FAITH (pp. 564–7); and *Control Devices* by K. M. RICHARDS (pp. 568–70).

None of these papers contains an appreciable amount of new material. Dr. Davis gives an interesting outline of an aspect of air pollution with which the readers of the *Bulletin* are probably unfamiliar, but the other authors' treatment is very sketchy. *J. McK. Ellison*

Occupational Hygiene

The order in this section is:—**General; Occupational Physiology; Occupational Diseases (Dust Diseases, Poisoning, Skin Diseases, Others); Occupational Psychology; Heating, Lighting and Ventilation.**

GENERAL

KEATINGE, G. F. **The Physician in Industry. The Wyers Memorial Lecture. 1960.** *Trans. Ass. Indust. Med. Officers.* 1961, Apr., v. 11, No. 1, 4–14. [37 refs.]

The Wyers Memorial lecturer introduces his subject by discussing the relationship between the factory worker and the physician at the factory. His subject however is not just the duties of the factory physician: it is the attitude he should adopt to his duties, and what he may expect to achieve.

Treatment of injury and illness at work is mostly passed on to the personal doctor or to a hospital staff. The role of the doctor in industry is to keep the medical and nursing staff and first-aid personnel efficient and up to date. Routine medical examinations come in for considerable criticism. Placement examinations, except where there are special requirements, are of limited value and could be replaced by a health interview carried out by an experienced nurse. The office of Appointed Factory Doctor for the purpose of examining and certifying the fitness of young persons has become almost an anachronism. Follow-up examinations are limited in Britain to executives (preferably to be called "officials") but the merits of such examinations are few. All persons reaching the retiring age of 65 are seen, and if they are continuing work, suitable jobs can be arranged.

Despite his criticisms, Dr. Keatinge admits that he carries out all these examinations: he believes in personal contact with the worker, having a "cosy chat," and is convinced that his most important function is that of a builder of morale. This question of morale is vital when a patient is absent from work because of injury or illness. With the agreement of those responsible for treatment, the industrial physician should visit him in hospital and maintain contact with him and his advisers after his discharge. This is most important, for the time which elapses before return to work depends on the advice given to the patient. The industrial physician can use his influence with general practitioners and surgeons in shortening convalescence. Experience of the Butterley Company is quoted to show that those who returned early to work suffered no ill effects. Specialized departments for the rehabilitation of the injured are considered something of a danger. Morale is more likely to be enhanced if the man continues to work with his mates in a normal production shop. Dr. Keatinge sums up his opinions on this subject by saying that he is something of a nihilist about certain aspects of rehabilitation.

The necessity of keeping adequate records and the use to which they can be put is demonstrated in 2 ways. It was found from the records of 3 groups of workers —quarrymen, farmers and foundrymen—that long hours of work did not increase the sickness rate. On the question of the accident prone, the records of those people with a susceptibility to small accidents showed that they had no greater liability to sustain serious accidents than others. This observation, so contrary to present ideas, is being investigated further. The observed differences in minor accident records reflect differences in the reporting of accidents by individual people rather than differences in their proneness to accident.

This rather bald summary does not do full justice to the lecturer; the lecture is extremely stimulating and should be studied by every industrial physician. Dr. Keatinge is to be congratulated on the excellent and candid presentation of his views.

Charles L. Sutherland

MATHEW, G. G. **The Training of Occupational Hygienists.** *Ann. Occup. Hyg.* London. 1961, June, v. 3, No. 4, 272–7.

CHEST & HEART ASS. **The Transactions of the Second Conference on the Health of Executives held in The Royal Festival Hall, London, 24th November, 1960.** 112 pp. 1961. London: Tavistock House North, Tavistock Square, W.C.1. [15s.; $3.50.]

This Annual Conference is held primarily for industrial executives and sets out to improve the health and education of this very limited occupational group. The report of this, the second conference, therefore must be assessed within these restricted terms of reference; some contributions succeed admirably, others are less successful and a few seem to be frankly irrelevant.

There has grown up within the last decade an assumption that the business executive is exposed to unique occupational health hazards, that these must be vigorously counteracted, and such a conference is one method of doing this. Yet there is little evidence available to support such an hypothesis, and one is left with the impression after reading these transactions, that there is much smoke but the fire beneath it is barely smouldering. L. G. NORMAN (pp. 7–15), with lucidity, says as much in a studiously factual manner. He brings clarity and reason to bear upon this highly emotional topic.

S. ALSTEAD (pp. 64–71) examines the patient-doctor complex with care and kindliness and should have succeeded in giving his listeners some insight into their own reactions when facing a medico. A. L. ABEL (pp. 81–89) gives a robust and jovial account of the value of surgery and surgeons, his advice is sound but it is doubtful if his breeziness would continue to support the anxious candidate for surgery further than the

confines of the Royal Festival Hall. More specifically the problems of coronary thrombosis are faced squarely and calmly by P. Dudley WHITE (pp. 50–63). Objectively and fully the epidemiology, pathology, clinical control and treatment are explained in the simplest and clearest of terms. This contribution is an object lesson in the art of health education to those pundits who can so frequently bewilder and terrify their listeners. The dynamics of psychiatric disorder in individuals and groups is tackled by D. O'NEILL (pp. 72–80). This whole field is much too broad to be handled in this way and before such an audience. The contribution is superficial and can have done little to relieve that suspicion of the psychiatrist's function which is endemic in the upper reaches of industrial management, an occupational stratum where so often his skills are sorely needed. H. M. SINCLAIR (pp. 21–32) produces an articulate account of many of the unsolved contemporary problems of nutrition existing in the more highly industrialized countries. It is marred by a heavy emphasis on some of the more speculative aspects of the effects of modern dietaries and by a vigorous piece of special pleading for a National Institute of Human Nutrition to perform fundamental research.

Less immediately relevant to the theme are two contributions; One from P. J. LAWTHER (pp. 16–20) on air pollution is a succinct and valuable account of the damage—human and material—caused by our insanitary habits. The other, an account of the functioning of the Health Service in the Port of London, given by J. G. WILSON (pp. 33–40), seems somewhat inappropriate. From the strictly medical point of view the most valuable contribution comes from A. D. BONHAM-CARTER (pp. 41–48). As a prominent industrial manager, he examines the work of doctors in industry. This statement can be read and re-read with value as it sets the future goals for the occupational health services of the larger units of industry in Britain.

The true value of such conferences still remains in doubt. Until the hazards, if any, which bedevil life in high places are more fully investigated, reported, understood and accepted, the programme for succeeding conferences must become increasingly repetitive or less immediately relevant. *W. T. Jones*

SORSBY, A. **Employment of the Partially Sighted.** *Trans. Ass. Indust. Med. Officers.* 1961, Apr., v. 11, No. 1, 39–42.

The author makes a plea that it is better to indicate the relatively few jobs that are unfitted for partially-sighted persons in preference to looking around for jobs which are considered suitable. He also stresses that more myopes go blind from chorioretinal degeneration than from retinal detachment, and to restrict the type of work done by myopes to that in which there is no heavy manual labour is putting an unfair burden on them.

[The reviewer is not entirely in agreement on this point. He has seen so many myopes who were never told of the dangers of heavy manual labour and who ended up with retinal detachment in one or both eyes which need not have occurred if they had led a more sedentary existence.] *D. P. Choyce*

OCCUPATIONAL DISEASES

JÖTTEN, K. W. & KLOSTERKÖTTER, W. [Edited by.] Die Staublungenerkrankungen. Vol. 3. Bericht über die 3. Internationale Staublungen-Tagung des Staatsinstitutes für Staublungenforschung und Gewerbehygiene beim Hygiene-Institut des Westfälischen Wilhelms-Universität Münster/Westf. vom. 29. bis 31. Oktober 1957. [**Dust Diseases of the Lungs. Report of the 3rd International Congress on Dust Diseases of Lungs, Institute for Investigation of Dust Diseases of Lungs and Industrial Hygiene, Institute of Hygiene Westphalia, Wilhelms-University Munster, 29–31 October, 1957**] pp. xvi + 607, 319 figs. [Numerous refs.] 1958. Darmstadt: Dr. Dietrich Steinkopff Verlag, Holzhofallee 35, Germany. [DM 65.]

This is a report of the papers presented to the Third International Pneumoconiosis Conference, held in Münster, Germany, in 1957, and the discussions which followed. It is divided into the following sections: (A) Fundamental research; (B) Animal experiments; (C) Electronmicroscopy; (D) Dust measurement; (E) Emphysema, bronchitis and silicosis and (F) Miscellaneous papers. The papers are mostly in German.

The 15 papers on fundamental research mainly describe evidence for or against various theories which attempt to explain the aetiology of silicosis. It is a commentary on the present state of our knowledge that such widely differing theories can all find their adherents, but no theory can yet be regarded as supported by satisfactory evidence.

The papers concerned with the solubility theory deal with the dissolution of silica in water and the nature of the solute produced. The ultrafiltration of polysilicic acid (7, H. STEGEMANN, pp. 93–98) [the numbers in parenthesis indicate the number given to the paper in this volume] yields a filtrate in which the molybdate-reactive silicic acid (mainly orthosilicic acid) is independent of the pore size of the filter (range 5 to 300 $m\mu$), being always about 0·14 mgm. per ml. (a value confirmed in paper 19). The monosilicic acid in a suspension of quartz in water never reaches this value. After treatment with HF, the amount of orthosilicic acid increases with pore size above 35 $m\mu$. This effect allows the mono- and polysilicic acid to be estimated. A suspension of an extremely fine silica powder in water gives mainly the simple silicic acid in solution.

The polymerization of silicic acid was studied by

using paper chromatography to separate the polymer fractions (8, H. BAUMANN, pp. 99–110). Below *p*H3 silicic acid is found to behave as a condensed acid. At neutral and alkaline *p*H, it exhibits the kinetics of a polymerization reaction. In neutral solution the polymerization reaction goes first through an induction period which is longer as the initial concentration is smaller.

In an effort to explain why quartz yields both mono-silicic acid and more complex polymers when it dissolves and to explain an initial phase of rapid solution, defects in the silica lattice have been studied (3, J. A. WADDAMS, pp. 40–52). Evidence is presented that silica surfaces are crazed but that the lattice defects are less common in the interior of the particles.

Amorphous silica in the lungs presumably is derived from silicic acid formed by the dissolution of siliceous dust. The air-dried dust from silicotic lungs was found to contain 6–7% of amorphous silica (6, A. WEISS, G. REIFF and G. HOFMANN, pp. 79–92) in cases graded as Silicosis III but the value was lower when the disease was of grade I. A discussion of the source of the amorphous silica brings esters of silicic acid into the picture and in this connexion studies of the interaction of catechol and other phenols with various types of amorphous and crystalline silica are described.

Interest is shown in the adsorption of a number of physiological substances to silica surfaces and in the interaction of such substances with mono- and poly-silicic acid, the assumption being that the removal or modification of some essential substance may initiate the fibrotic process. A purely physico-chemical study of the heats of adsorption and isotherms associated with the adsorption of a number of substances is described (2, W. STÖBER and G. BAUER, pp. 31–40).

The orientation of certain amino acids on quartz, crystobalite, tridymite, talc and graphite surfaces (1, H. SEIFERT, pp. 3–26) and the adsorption of albumin to water-, acid- and alkali-extracted quartz (5, W. LICHT, pp. 72–76) has been observed, the results being used to support the matrix theory which assumes the build-up of fibres on protein adsorbed on the silica surface.

Although no action of silicic acid on the succinic-acid—cytochrome system could be demonstrated, oxygen adsorption through the cytochrome-oxidase—cytochrome-c system was found to be reduced by silicic acid in concentrations of 0·2–0·6 mgm./ml. Cytochrome-c is denatured by polymerized but not by mono-silicic acid (11, R. NICOLAS, pp. 125–139). Mono-silicic acid is reported to reduce the activity of glucose-6-phosphatase (10, W. KERSTEN, K. KRISCH and H. STAUDINGER, pp. 117–123), an effect which might interfere with the energy requirements of the cell.

VIGLIANI's immunological theory, which classifies silicosis with the collagen diseases, is now well known, and the theory has been described in English [this *Bulletin*, 1959, v. 34, 347]. A short introductory paper (12a) by E. C. VIGLIANI (pp. 143–147) deals with the proteins of silicotic tissue. Of the hyaline material, perhaps half is of non-collagenous proteins. B. PERNIS (12b, pp. 147–153) describes immunological experiments with rabbits, and G. MOTTURA (12c, pp. 153–158) histopathological studies on rats which had inhaled silica. Mottura concluded that the changes observed—histiocyte proliferation, necrosis and plasma changes—are best explained by assuming an immunological process. The accumulation of quartz particles could be accompanied by sensitization, followed by the liberation of pulmonary antigens; but the quartz might also produce antigens by structurally modifying adsorbed substances. By a different technique (13, M. ANTWEILER and E. HIRSCH, pp. 161–168) quartz with adsorbed homologous serum albumin was shown, by agglutination tests, to produce antibodies when injected into rabbits. Similarly treated cristobalite, tridymite and vitreous silica were less active and diamond, aluminium, aluminium phosphate, iron and iron oxide were inactive. Agglutination tests on human subjects were reported to have given only one positive among 20 healthy persons but about two-thirds of the miners and silicosis patients tested gave positive reactions.

The quantitative determination of the fibrogenic activity of dust continued to receive attention. It was reported (16, J. GLÖMME, pp. 176–181) that a direct weighing of the lungs of rats which had received quartz could be a satisfactory measure of the degree of fibrosis induced, and (17, D. RIVERS and T. G. MORRIS, pp. 181–189) that the fibrogenic activity of a dust can be assessed by injecting a known weight of dust into the tail-vein of a mouse and assessing the fibrosis induced in the liver. Experiments (19, J. CHARBONNIER) with silica dusts of mean diameters 81, 265 and 595 Å respectively generally confirmed the results of others in that the rate of solution and general toxicity of silica dust are proportional to the surface area, but that fibrosis is induced in animals only by the coarser material. These results are explained by the older solubility theory.

Other experiments (22, W. KLOSTERKÖTTER, pp. 236–247) with several forms of silica led to the conclusion that crystalline silica and amorphous silica heated above 800°C. are fibrogenic, that polysilicic acid has only a primary toxic, proliferative and fibroplastic effect, and that a silica condensate formed above 2,000°C. has an intermediate action. It was concluded that crystallinity and alteration by heat favour fibrogenic activity.

Inhaled quartz dust is found distributed through the lungs of rats in a manner comparable with that found in man (26, K. D. FRIEDBERG, pp. 286–291)—that is, most is in the upper and least in the lower lobe. If the dusting is light the mechanism of removal *via* the bronchial tree is efficient and no dust is found in the tracheobronchial lymph nodes. However, the particles of a silica aerosil, the surface of which had been esterified to make it hydrophobic, was rapidly transported to the lymph nodes (27, F. J. STRECKER, pp. 291–294). The different behaviour is regarded as due to the difference in particle size. The toxicity of surface-coated Aerosil has also been studied (20a, F. J. STRECKER, pp. 220–226). When administered to mice by intraperitoneal injection of a suspension or implantation of the dry powder, the more water resistant surfaces were less lethal. Thus the toxic action decreased with the chain length of the alcohol used to esterify the surface, and when surface-esterified with trimethylsilyl group, the

silica was non-toxic in 60 mgm. dose. Slight temporary fibrosis was demonstrated.

Two papers discuss metals in silicotic lesions. The one (14, F. TIMM, pp. 170–172) deals with the trace metals zinc, copper, iron and lead; the other (15, R. NETH, 173–175), of histochemical interest, reports that iron was not demonstrated in a granuloma produced by iron-free quartz.

On coal-workers' pneumoconiosis the opinion is expressed (32, G. NAGELSCHMIDT, 329–336) that massive fibrosis results if the lung contains a large quantity of coal dust; the small quantity of quartz which may also be present is regarded as insignificant. However, animal experiments are described (31, W. KLOSTERKÖTTER, M. T. MACKOWSKI, E. SCHILLER, H. W. SCHLIPKÖTER and A. THAER, pp. 312–326) to show that small additions of quartz made to various grades of coal dust enhanced the fibroblast reaction and a difference could be detected by histology. Coal dust was shown to enhance the pathogenicity of tubercle bacilli in the lungs of guinea-pigs (33, E. J. KING, foreword by C. V. HARRISON, pp. 336–345) and progressive massive fibrosis was considered to be chronic tuberculosis in a dusty lung.

Emphysema and bronchitis in coal-workers has evidently received considerable attention as is evidenced both by the papers and the lengthy discussions. Respiratory symptoms—bronchitis and lowered ventilatory capacity—are among those shown by coal-workers in South Wales when compared with the non-mining population (47, J. C. GILSON, pp. 491–498), and another paper (40, K. HUSTEN, pp. 396–414), which classified the causes of emphysema, indicates that autopsies showed more emphysema even in miners without silicosis than in the general population. The emphysema was more severe in miners with silicosis. However, a paper from Holland (48, A. V. M. MEY, 498–504) indicates that it is not yet decided whether emphysema and bronchitis represent an occupational disease of coal-miners, and similarly a survey in Germany (41, G. WORTH, pp. 414–435) showed that emphysema was absent in men with less than 15 years' exposure to dust underground and that later development may not be due to dust. Animals have been used in the working places to follow pathological changes due to dust (42, E. SCHILLER, pp. 435–441).

A method of following abnormalities in the respiration in silicosis (43, H. DEENSTRA, pp. 441–444) and a paper correlating respiratory pattern and the composition of blood gases (44, H. VALENTIN, pp. 444–458) are presented. Another feature of possible diagnostic value is the 17-ketosteroid level in the urine. The level was found to be markedly reduced in coal-workers with rapidly developing early silicosis or with advanced silicosis (62, A. HILGERS, pp. 576–588). The origin of cor pulmonale is discussed (45, J. R. RÜTTNER and R. GASSMANN, pp. 459–470).

The control of pneumoconiosis in some sections of German industry includes X-ray screening (50, H. BUCKUP, pp. 510–519) and younger men who show lung changes are transferred to other occupations. On the experimental side, aerosols of aluminium hydroxide and hydroxychloride were found to have an inhibitory action on the production of fibrosis in rats (63, H. LÜCHTRATH, pp. 588–594); ferric chloride is much less active. The inhibition in rats of quartz-induced fibrosis by cortisone was demonstrated by chemical estimation of silica and collagen in the tissues (18a, b, B. D. STACY and E. J. KING, pp. 189–197, 197–209). Vitamin B was also said to be inhibitory (4b, J. MÜLLER, pp. 58–67).

Electron microscopy has been applied to the dust problem in a number of ways. The histological changes following the intraperitoneal administration of a silica condensate, silica gel and quartz were studied (37, W. KLOSTERKÖTTER and H. THEMANN, pp. 373–382) by this means as an extension of the knowledge given by light microscopy. Only histiocytes appear to act as phagocytes in the silica granulomata produced by the intratracheal injection of a silica condensate (36, A. POLICARD and A. COLLET, pp. 368–373). Silica particles coated with denatured cytoplasm were less toxic than uncoated particles and it was assumed that silica alters the cytoplasmic proteins. Silica was shown to cause the mitochondria to swell in the cells of a rat's lung (35, W. KIKUTH, pp. 353–367).

Electron microscopy has been used to follow the deposition of submicron (0·1–0·2μ) dust in the human lung (28, L. DAUTREBANDE, H. BECKMANN and W. WALKENHORST, pp. 297–307). The dust deposition, measured by examining the tidal air, was found to be inversely proportional to the respiratory rate, but in the deep pulmonary regions the deposition is not influenced by the respiratory rate. Up to 90% of the dust was stated to be removed in the alveoli.

Pneumoconiosis in certain industries is described. The silicosis of porcelain workers develops slowly. The oxygen value of the arterial blood and the lung changes shown by X-ray are related to the time following the first exposure to dust rather than to the length of exposure (49, N. ZÖLLNER, pp. 504–509). Silicosis in the firebrick industry develops more rapidly because the dust has a high silica content (over 90% SiO_2). A progressive worsening of lung function has been observed (64, B. BUGYI and F. BURKART, pp. 594–600). Animals were used to compare the properties of dust from a works using ferrosilicon (A, 60 mμ particles) with amorphous silica (B, 100 mμ), quartz (C, 1250 mμ) and titania (D, 100 mμ) (21, J. GLÖMME and A. SWENSSON, pp. 231–235). After intraperitoneal injections, the amount of silica excreted in the urine varied in the order B $\geqslant$ A and C. After intravenous injection the order of toxicity was A and B $>$ C and D and the ability of the dusts to produce fibrosis in the lung during 8 months was in the order C $>$ B $>$ A $>$ D.

Pneumoconiosis due to dust in the tungsten carbide industry is discussed (54, E. W. BAADER, pp. 531–536), and (55–60, L. DÜNNER, pp. 541–544; E. WENDE, pp. 545–550; H. J. LÖBLICH, pp. 550–556; G. SEPKE, pp. 556–560; H. MÜLLER, 561–564; J. C. WAGNER, pp. 566–569) in workers handling flour and grain, diatomite and kaolin.

Only two papers deal with the measurement of dust, the one (38, L. LE BOUFFANT, pp. 385–389) describing the use of the micropore filter and the other (39, M. LANDWEHR and G. PFEFFERKORN, pp. 390–395) a procedure for the evaluation of konimeter and thermal precipitator samples with the light and electron microscopes.

Die Staublungenerkrankungen gives a good cross-section of the work in progress in Europe and outlines current ideas on pneumoconiosis. Although most of the work has now been recorded in more extended form in the journals, this volume can be regarded as a valuable index to current research. *P. F. Holt*

KAST, W. Neues Staubmessgerät zur Schnellbestimmung der Staubkonzentration und der Kornverteilung. [**A New Apparatus for Rapidly Determining the Concentration and Sizes of Dust Particles**] *Staub.* Düsseldorf. 1961, Apr. 26, v. 21, No. 5, 215–23, 18 figs.

This sampling device consists of a flat spiral channel mounted on a perpendicular axis common to an air suction fan, with an electric motor and a compressed air turbine as alternative drives. Air for sampling is drawn in at a rate between 5·9 and 7·5 m^3 per hour at rotation speeds of 3,000 and 4,000 r.p.m. The outer wall of the spiral is covered with a strip of thin aluminium foil. Air enters at the centre of the spiral and travels outwards, depositing particles by centrifugal force along the channel, the heavy ones near the centre and the lighter ones towards the periphery. Particles down to 0·5–1·0 micron diameter are collected. The foil can be stripped out and 5 sections of it weighed to find the amount of dust deposited at different distances along its length.

The mathematics of the system is worked out and a correction curve given for the departure of heavy particles from Stokes's law of drag. The theoretical expression relating particle size and density to the limiting point of deposition shows that the latter is liable to be uncertain for the larger sizes so the apparatus was calibrated with dusts which had been fractionated by the Andreasen method.

Examples are given of cumulative size distributions; dust concentrations were in good agreement with parallel determinations in which filters were used.

C. N. Davies

BRUCKMANN, E. Röntgenographische Mineralbestimmung von atembaren Schwebestäuben. [**X-Ray Determination of Minerals in Respirable Dusts**] *Staub.* Düsseldorf. 1961, June 1, v. 21, No. 6, 247–51, 6 figs. [13 refs.]

The English summary appended to the paper is as follows:—

"A simple method for X-ray determination of minerals in respirable dusts is described. The dusts $< 5\ \mu$ collected in scrubbers are precipitated by filtration on membrane filters in the method employing admixtures of calibration substances and analyzed. When using membrane filters and the pre-impinger the dust sample collected on the filter can be analyzed by the comparison method without further preparation. In this case, gravimetric determination of the dust concentration and determination of the X-ray absorption coefficient of the sample occur simultaneously. Routine analyses can be carried out with quantities of dust from 10 mg. upwards."

THOUZEAU, G. & TAYLOR, T. W. **The Physical Properties of Colliery Stone Dusts.** *Safety in Mines Research Establishment.* [Portobello St., Sheffield, 1.] *Research Rept.* No. 197. 1961, Feb., 28 mimeographed pp., 6 figs. [3s. 3d.]

SCHNITZLER, H. & SOMOLYAI, J. Einfluss der elektrischen Aufladung auf die Koagulation von Staub. [**Influence of Electrical Charge on the Coagulation of Dust**] *Staub.* Düsseldorf. 1961, June 1, v. 21, No. 6, 241–6, 11 figs. [24 refs.]

The English summary appended to the paper is as follows:—

"A process is described which makes it possible to measure the relationship between electrical charge and coagulation of a dust cloud under climatic conditions that are maintained constant. The distribution of falling velocity is measured by means of a recording electrical micro-balance of the GAST type. At the same time the state of charge of the entrained dust is recorded separately by positive and negative charges by using a double condenser and two electrometer amplifiers. Some current qualitative results are reported. The work is proceeding."

NATIONAL COAL BOARD. **Medical Service. Annual Report 1959** [ROGAN, J., Chief Medical Officer]. 12 pp. [1960.] London: Hobart House, Grosvenor Place, S.W.1.

The periodical chest X-ray scheme came into full operation in all Divisions in 1959, and 78·7% of the total number at the collieries surveyed submitted themselves voluntarily for examination. It is clear that pneumoconiosis is a problem common to all coalfields, but that its extent varies markedly fom one to another. Pneumoconiosis of Category 1 (early dust retention) varied from 34·2 to 152·9 per 1,000 men (average 79·1) in the 8 areas. Categories 2 and 3 from 12·7 to 97·7, and progressive massive fibrosis from 1·6 to 33·2. Most of the positive results were in men over 35 years old. The highest rates in general were in men from the Durham Division, the North-Eastern Division, the West Midlands Division, and (highest) the South-Western Division. The number of new cases of pneumoconiosis reported was an increase over the number for the previous year, as a result of this X-ray scheme; a greater rise is predicted for 1960.

Large numbers of dust measurements are recorded, and there has been an increase during the past few years in the number of working places which meet approved standards.

There has been no real increase in the prevalence of the beat diseases, dermatitis and nystagmus in the past 3 years.

13 more medical centres were built in 1959, bringing the total to 368, and (excluding staff wholly employed on medical research) the Board employed 72 doctors, 368 nurses and 2,370 medical room attendants during the year. In 1959 over 19,000 men with pneumoconiosis continued to be employed by the Board; in only 121

cases was the Board unable to make work available for them in suitable dust conditions. *Charles Wilcocks*

ROGAN, J. M. **Chest Disease in Coalminers, with special reference to the Pneumoconiosis Field Research.** Reprinted from *Mining Engineer*. 1960, Nov., No. 2, 107–14, 2 figs. [15 refs.] Discussion 114–18.

This paper commences with a history of dust disease in coalminers in Britain. The early history is derived from papers by MEIKLEJOHN [this *Bulletin*, 1952, v. 27, 64, 939].

The important date in the later history is 1948, when miners suffering from pneumoconiosis were allowed to continue to work in the coalmining industry either on the surface or underground in "approved" dust conditions. The "approved" conditions were agreed upon as follows:—

	Size range
Stone dust—450 particles per cc.	0·5 to 5 microns
Anthracite—650 particles per cc.	1 to 5 microns
Coal —850 particles per cc.	1 to 5 microns.

These approved conditions cannot be taken as certainly safe so research was instituted to establish safe conditions on a firm scientific basis.

The Pneumoconiosis Field Research was set up in 1952 to study the dust conditions in 25 collieries throughout the country along with radiographic examinations of the workers in these collieries. Repeated sampling of the dust has provided a continuous exposure history for each of the 35,000 men in the research. Mobile X-ray units were employed making full-sized films. Techniques of recording X-ray films were devised to minimize personal variations in reading. The intention at first was to establish a dust level which would fail to produce radiological appearances within the working life of the great majority of mineworkers. The research has been extended to obtain information about chest symptoms and disability. Examinations at 8 collieries have been completed in the second round. Each man was given a questionaire of chest symptoms and to estimate disability each man was tested for the Forced Expiratory volume of 1 second [GAENSLER, *Science*, 1951, v. 114, 444].

The results showed that simple and complicated pneumoconiosis were much more prevalent in South Wales than in other coalfields. Variations in prevalence were found in other coalfields and even in collieries in the same Division. The information gained from the second round is that a high prevalence of symptoms was associated with a high prevalence of pneumoconiosis and *vice versa*. The effect of respiratory symptoms on lung function is rather less in men with pneumoconiosis than it is in men with respiratory symptoms and normal X-rays. It will not be possible to establish criteria for safe dust conditions until some time after the completion of the third medical survey. In the meantime to show the effect of dust suppression and so give assurance to men and management, a regular periodical X-ray examination of miners was introduced in 1958.

This paper was read before the Institution of Mining Engineers on June 29th, 1960 and the discussion which followed touched on topics such as aluminium prophylaxis, effect of smoking, types of physique, the use of medicated sprays and aerosols, etc. Attention was also drawn to the low incidence of pneumoconiosis among young miners as shown by the Ministry of Power Statistical Digest 1958 [this *Bulletin*, 1961, v. 36, 434]. Dr. ROGAN pointed out that young workers were likely to be unaware of pneumoconiosis, and that compensation figures do not give a true incidence. Information will shortly be available from the periodic X-ray scheme which will suggest a need for more intense dust suppression in parts of the South Wales coalfield. *Charles L. Sutherland*

ROGAN, J. M., ASHFORD, J. R., CHAPMAN, P. J., DUFFIELD, D. P., FAY, J. W. J. & RAE, S. **Pneumoconiosis and Respiratory Symptoms in Miners at Eight Collieries.** *Brit. Med. J.* 1961, May 13, 1337–42, 7 figs. [31 refs.]

On the basis of 5 comparatively small sample surveys [this *Bulletin*, 1956, v. 31, 1233, 1234] it has been suggested that pulmonary disability among coal miners is not due to simple pneumoconiosis but rather to "chronic bronchitis" which is unduly prevalent in the mining population. The plan of the study being undertaken by the Pneumoconiosis Field Research Unit of the National Coal Board was accordingly modified by supplementing the radiological examination of each man at 25 pits by a determination of the volume of air expired during the first second of a forced expiration after a full inspiration (FEV_1) and by a questionary of respiratory symptoms. Some of the findings of the modified medical surveys at 8 out of the 25 collieries are now reported. 3 collieries in Scotland, 2 in England and 3 in South Wales, about 9,000 men in all, were studied, representing over 90% of the working population at each colliery except one of the Scottish pits where the figure was 86·8%. A full size—14 × 14 inches—postero-anterior chest X-ray film was taken of each man. The International Labour Organisation (1953) Classification of Pneumoconiosis [*ibid.*, 1954, v. 29, 626] was used. The prevalence of pneumoconiosis Category 1 or more increased with age, and varied from 9·1 to 41·1% from one colliery to another. The FEV_1 tended to fall as the X-ray category rose. The fall was very small in the lower categories, but larger in Category 3 and in progressive massive fibrosis. The prevalence of respiratory symptoms increased with age and varied from 16 to 43·1%. The mean FEV_1 of men with respiratory symptoms was age for age about 0·2 to 0·4 litre less than the mean FEV_1 of men without respiratory symptoms; the difference increased among the older men. The prevalence of pneumoconiosis showed some association with the prevalence of respiratory symptoms. In the higher X-ray categories more men complained of respiratory symptoms than in the lower. Men without respiratory symptoms showed a fall in FEV_1 with increasing X-ray category. This effect was absent in men with respiratory symptoms. Respiratory symptoms

were associated with a smaller fall in the FEV_1 in men with pneumoconiosis than men with normal X-ray pictures. Irrespective of the presence or absence of pneumoconiosis and respiratory symptoms, the FEV_1 fell uniformly with age.

It is pointed out that while detailed comparison of these results with those of other workers should be made with care, nevertheless the prevalence of Category 1 or more pneumoconiosis is consistent with the results of earlier surveys [*ibid.*, 1956, v. 31, 414; 1957, v. 32, 256]. The relatively small increase in dyspnoea with an increasing degree of simple pneumoconiosis (save for older men with Category 3 pneumoconiosis) which was noted accords with the findings of GILSON and HUGH-JONES [*ibid.*, 1956, v. 31, 825] and is not dissimilar to those of LAVENNE (*C.R. Journées Françaises de Pathologie Numière*, 1961, in press). To the best of the authors' knowledge, the association between the prevalence of pneumoconiosis and that of respiratory symptoms has not been observed before for a complete working population, and various hypotheses are discussed to account for the finding that respiratory symptoms in men without pneumoconiosis are associated with a greater fall in the FEV_1 than in men with pneumoconiosis. *G. F. Keatinge*

PAUL, R. **Chronic Bronchitis in African Miners and Non-Miners in Northern Rhodesia.** *Brit. J. Dis. Chest.* 1961, Jan., v. 55, No. 1, 30–34. [15 refs.]

3,536 African miners and 1,815 non-miners attending the Pneumoconiosis Medical and Research Bureau in the early part of 1959, were questioned about the presence of persistent cough with sputum and about their smoking habits. The diagnosis of chronic bronchitis was made on an affirmative answer to the first question even in the absence of physical signs, if no other reason for these symptoms was present, and the cases were investigated further. There were only 5 cases in the miners (all in the older men) and none in the non-miners. 35% of the miners had exposures of more than 10 years.

In a group of 675 deceased miners examined *post mortem*, and dying from all causes (including injury in more than 50%) there were 16 in whom chronic bronchitis was diagnosed. Cases showing minimal changes were included, and in only 2 had there been symptoms of cough and sputum. The disease was found in both young and old men, and 10 of the 16 were miners with less than 5 years' exposure to dust. A table shows the comparison of the author's results with those recorded by workers in 3 areas in Britain [this *Bulletin*, 1957, v. 32, 50; 1958, v. 33, 238; 1959, v. 34, 238].

Smoking habits were moderate, and the population surveyed, when not at work, lived in an unpolluted atmosphere completely devoid of fog. The author considers that the extremely low incidence of chronic bronchitis in the miners is evidence against the contention that dust is an important predisposing factor [*ibid.*, 1960, v. 35, 850]: many factors are probably involved, of which smoking and atmospheric pollution are probably noteworthy. *A. T. Doig*

AHEARN, V. P., SANDER, O. A., VORWALD, A. J., WRIGHT, G. W. & HARTMAN, W. C. **Emphysema Pneumoconioses and Compensation. A Panel Discussion.** *Arch. Environment. Health.* Chicago. 1961, Mar., v. 2, No. 3, 307–26.

The author as the moderator posed the questions: replies were given by Dr. O. A. Sander as clinician, Dr. A. J. Vorwald as pathologist, Dr. G. W. Wright as physiologist and Mr. W. C. Hartman as a legal adviser. The compensation and legal part of the discussion is of interest mostly to the American reader. The discussion on emphysema and pneumoconiosis and their relationship was elicited by a number of the questions, and produced in some matters variations in the views held. The difficulty of giving a definition of pneumoconiosis was shown by the views put forward. Sander said that we all had pneumoconiosis ever since the first dust particle was picked up by a phagocyte and retained in the lung. Wright felt that a term which connotes disease should not include any situation compatible with what we call "health". Vorwald considered it a generic term which connotes a pulmonary condition provoked by the presence of inorganic dust in the lung. It bears no reference to clinical manifestations in terms of health and disease. He mentions the definition in the National Insurance (Industrial Injuries) Act 1946 in Great Britain as showing that his view is not generally accepted. [This brings to mind the fact that this British definition was much criticized but the Committee which discussed it [this *Bulletin*, 1953, v. 28, 1060] decided that any definition would be subject to objection.]

The diagnosis of emphysema was fully discussed. In diffuse obstructive emphysema, Wright required a triad of physiological findings, subnormal maximum breathing capacity, elevated residual volume and abnormal pulmonary ventilation as demonstrated by using helium or other foreign gas; but even in the presence of this triad the diagnosis is not always certain. All were agreed that the basic cause of any of the forms of emphysema was unknown. Sander said that it has never been proved that disabling emphysema can result only from occupational dust exposure. Vorwald considered that emphysema is provoked by the pulmonary deposition of dusts in certain industrial processes, instancing focal emphysema in coal workers' pneumoconiosis, bullous emphysema of bauxite workers and the emphysema induced by the contraction of massive fibrotic lesions. Both Sander and Wright considered that minimal nodular silicosis was not a cause or contributory factor when a well developed emphysema is associated with it. Wright mentioned diffuse obstructive emphysema in this connexion. Later, in replying to another question, he affirmed that with one exception he knew of no evidence to implicate dust as a cause of diffuse obstructive emphysema. The exception was its occurrence along with progressive fibrosis.

To the question "*Can pneumoconiosis produce primary thrombi or infarction in the vascular system of the lungs?*" Sander and Wright replied "no". Vorwald on the other hand stated that a pneumoconiosis of the active type, which induces significant inflammatory reaction with the production of massive

fibrosis, can produce thrombosis of vessels with consequent infarction of the lung.

Other matters discussed were the assessment of partial disability, the treatment of pneumoconiosis, the association of cancer with either emphysema or pneumoconiosis, and the possible disability from benign pneumoconiosis. *Charles L. Sutherland*

BYERS, P. D. & KING, E. J. **Experimental Infective Pneumoconiosis with Coal, Kaolin and Mycobacteria.** Reprinted from *Lab. Investigation.* 1959, May–June, v. 8, No. 3, 647–64, 8 figs. [46 refs.]

The literature on natural and experimental pneumoconiosis is reviewed, and the results of 2 experiments with guineapigs are described. In the first a chromogenic mycobacterium of low virulence was injected intratracheally into guineapigs, alone and with coal dust or kaolin. Some animals were treated with an antituberculous substance, Triton WR 1339. The result of Triton treatment of animals injected with the organism alone was to bring about complete regression of the lesion, but in those receiving dust and organism the effect was not very marked. The lesions produced by dust and organism were similar to the progressive massive fibrosis of coal workers, although they were less highly collagenized and regression of the lesions was observed to begin after about 105 days.

In the second experiment guineapigs were exposed to a total of 3,900 hours to a coal-dust-laden atmosphere, and then injected intratracheally with the vole bacillus, control animals being dusted only, or receiving only vole bacillus. The reaction of the dusted animals to bacilli was very much more severe than in those injected intratracheally in the first experiment. 50% of the animals died and regression was not apparently observed in the remainder. The difference in the amount of dust present or in its distribution in the lungs might be responsible for the greater severity of the reaction.

In all the experiments a condition resembling progressive massive fibrosis was produced, the amount of lung involvement usually ranging from 50 to 90% and gross cavitation being present. *A. T. Doig*

BYERS, P. D. & KING, E. J. **Experimental Infective Pneumoconiosis with *Mycobacterium tuberculosis* (var. *muris*) and Haematite by Inhalation and by Injection.** *J. Path. & Bact.* 1961, Jan., v. 81, No. 1, 123–34, 8 figs. on 4 pls. [20 refs.]

The authors, having produced lesions closely resembling progressive massive fibrosis in guineapigs and rats with coal dust and kaolin dust mixed with *Mycobacterium tuberculosis,* [above] decided to conduct similar experiments with haematite dust. They used finely ground haematite, 95·6% of the particles being less than 1·5μ. It was administered to one group by dusting and to another by intratracheal injection. For the dusting experiments 25 guineapigs were exposed either to a concentration of 55 mgm. per cubic metre for 3,838 hours, or to 46 mgm. per cubic metre for 4,157 hours. There were 17 survivors, 5 of which were kept as controls, the remaining 12 receiving 10^4 vole bacilli intratracheally. 18 animals were injected intratracheally with 100 mgm. of haematite mixed with 10^4 vole bacilli in 1 ml. saline, and other controls animals included 13 untreated, 10 injected intratracheally with haematite only, and 16 injected intratracheally with vole bacilli only. The experiments were planned to last 8 months: this was adhered to with animals intratracheally injected but the animals dusted with haematite mostly died or were killed within $3\frac{1}{2}$ months.

The animals dusted with haematite which did not receive tubercle bacilli showed little pulmonary fibrosis in spite of very high amounts of haematite in the lungs: similarly animals receiving intratracheal injections of haematite alone showed a minimal fibrous reaction. Vole bacilli alone produced only transitory disease. Both groups of animals which received haematite and vole bacilli developed extensive disease with widespread fibrosis. This was particularly severe in the dusted animals which had in their lungs about 6 times as much dust as the intratracheally injected animals and which received a more virulent strain of tubercle bacilli. The 12 animals so treated died within 10 to 106 days and all except 2 showed confluent lesions which were similar to the progressive massive fibrosis described in haematite miners. The animals which had been injected with a somewhat attenuated strain of tubercle bacilli likewise developed extensive disease with widespread fibrosis, but from 140 days onwards the lesions underwent regression, showing grade 1 fibrosis rather than grade 2.

[These experiments undoubtedly confirm that a combination of tubercle bacilli and haematite dust is more toxic than one or the other separately, but it is not certain how far the findings are applicable to the development of progressive massive fibrosis in man.] *A. T. Doig*

STEENKEN, W., JR., RALEIGH, J. W. & SMITH, M. M. **The Pathogenicity of Isoniazid-Resistant, Catalase-Negative Tubercle Bacilli for the Silicotic Host (Guinea Pig).** *Amer. Rev. Respiratory Dis.* 1961, Feb., v. 83, No. 2, Pt. 1, 208–12, 6 figs.

Twenty-three years ago GARDNER (*J. Amer. Med. Ass.*, 1938, v. 111, 1925) showed that an attenuated strain of tubercle bacillus gave rise to widespread chronic silico-tuberculosis in guineapigs with well established pulmonary silicosis. Lung tissue containing large numbers of tubercle bacilli removed from such animals failed to produce progressive disease when subinoculated into normal guineapigs. Since isoniazid-resistant, catalase-negative tubercle bacilli will not generally produce fatal disease when given subcutaneously, intravenously, or by inhalation to normal guineapigs, rabbits and monkeys, the present study was undertaken to determine whether such organisms would be capable of producing progressive disease in guineapigs with pulmonary silicosis when administered by the inhalation and subcutaneous routes.

10 strains of tubercle bacilli and 200 female guineapigs were used in the experiment. Half the guineapigs

were dusted with quartz for 8 hours a day, 5 days a week, for 8 months; dust counts showed an average of 500 to 900 million particles less than 10 microns in size per cubic foot of air. Animals which had well established pulmonary silicosis were paired with non-dusted controls and both groups were infected with the various strains of tubercle bacilli. When a dusted infected guineapig died, a non-dusted infected animal was killed for comparison. Those animals which had not died spontaneously of their disease were killed at the end of 18 months from the day of infection. Gross and histological studies of tissue and bacteriological culture were done on all animals.

Although marked silico-tuberculosis developed in the silicotic group, involving spleens and lymph nodes in addition to the lungs, infection of the non-dusted animals was generally limited in extent. Specimens of tissue from the lungs and spleens of animals in each of the groups were cultured for bacteriological and virulence studies. None of the recovered organisms produced progressive disease when subinoculated subcutaneously into the inguinal region of normal guineapigs or when given by inhalation. It is therefore deduced that tubercle bacilli highly resistant to isoniazid and which have lost their catalase activity and their ability to produce progressive disease in normal guineapigs, still have the power of producing progressive and at times fulminating disease in a silicotic host. Accordingly, isoniazid-resistant catalase-negative tubercle bacilli which do not produce progressive disease in experimental animals may not be innocuous to human beings and until more is known about the environmental effects upon infections produced by these organisms, caution should be exercised in undertaking human vaccination by attenuated organisms of this type, especially in those who may be exposed to quartz dust. *G. F. Keatinge*

AHLMARK, Axel, BRUCE, Torsten & NYSTRÖM, Åke. **Silicosis and other Pneumoconioses in Sweden.** 399 pp. illustrated. 1960. Stockholm: Svenska Bokförlaget, Norstedts, Sweden. London: William Heinemann Ltd.

This is in some respects a sequel to the excellent review of the silicosis situation in Sweden by BRUCE [this *Bulletin*, 1943, v. 18, 486]. The object of the book is to pave the way for the establishment of such efficient prophylaxis that the occurrence of new cases of pneumoconiosis will be prevented. Stress is laid on the fact that technical prophylaxis is all-important in eliminating the risk, but until such prophylaxis is perfected it must be supplemented by medical supervision.

This book is intended to bring up to date the experience of pneumoconiosis in Swedish industry from the medical angle. To achieve this object, the records of all cases notified in accordance with the laws of industrial insurance covering pneumoconiosis up to the end of 1956 were examined. The important details as regards exposure, stage of the disease, progression, etc. were collected. Two laws cover insurance for pneumoconiosis. Fibrosis of the lungs "due to silica dust or silica mixed with other dusts" was covered in January 1931. This cover was extended to other pneumoconioses "produced by the action of inorganic substances" in July 1950, thus including such conditions as asbestosis, berylliosis, hard metal pneumoconiosis, etc. The clinical material comprised 2,253 cases, the vast majority, 2,217, being of silicosis or mixed-dust silicosis. Compulsory medical examinations in the processes, and general radiographic surveys, played a large part in revealing silicosis and mixed-dust silicosis during the 1940's when the largest numbers were notified to the insurance authorities. There is often an interval between detection of slight pneumoconiosis and notification, and this is given as a possible reason for the small numbers notified in recent years.

All deaths up to the end of 1953 were investigated. 582 were in patients suffering from silicosis or mixed dust silicosis, 215 died from other causes such as cardiovascular disease (116), pulmonary cancer (16), and other pulmonary disease (19): 5 of the 36 notified under the 1950 law died of the occupational diseases.

The greater part of the book, 320 pages, is naturally taken up with the consideration of the occupations producing silicosis and mixed dust silicosis. These are divided into 5 main groups: (1) Mining, quarrying and tunnelling, (2) Steel and iron industry, (3) Ceramic industry, (4) Other industries and occupations (coal-mines; crushing of quartz, etc.) and (5) Work in two or more of groups 1 to 4.

Most cases came from the mining and the metal industries, and the ceramic and the mining industries had the highest proportion of deaths.

The method of presentation of the clinical material follows a set pattern in each occupational group within the main groups. The main headings are age, exposure period, stage of the disease at diagnosis, age at commencement of exposure, presence of tuberculosis, mortality, progression during continued exposure and after cessation of exposure; award of disablement benefit. The stages of the disease are based on a classification adapted from that recommended at Johannesburg in 1930 [*ibid.*, 1931, v. 6, 513]. Stage 1 is considered to be present when the lungs show pinhead-size opacities. Stage 2 when the opacities reach pea size, and Stage 3 when there is coalescence.

Coexistent pulmonary tuberculosis is only recognized after the demonstration of the bacilli in direct sputum smears, culture of sputum or by guineapig tests with gastric washings.

The silicosis found was mostly at an early stage at the time of diagnosis but in 400 workers the disease was more advanced. In 2 occupations, quartz crushing and sandstone metal grinding, there was a preponderance of advanced disease. The shortest exposure period at which Stage 1 was diagnosed was under 10 years, in miners at Laisvall mine—a quartz-rich lead mine—and in quartz crushers. The age at which silicosis is diagnosed depends to some extent on the age of entry into the dusty occupation. Potters shop workers showed signs of the disease after an exposure of 16 to 30 years and the age of commencing this occupation was under 20 years. Early pneumoconiosis following brief exposure was more common in women

pottery workers than in men. Pulmonary tuberculosis was a common complication in most of the occupational groups, possibly more common where the silicosis as such was severe. Among the 360 deaths there were 96 from silicosis and tuberculosis, 136 from silicosis alone.

The progression of silicosis during continued exposure was found to be slight in iron moulders and high in quartz crushers, and generally speaking progression was more evident the greater the content of quartz in the dust. Cessation of exposure did not ensure arrest of the pneumoconiosis. The authors' comment on the findings in regard to progression is:—"Not even such a drastic measure as removal from the dusty work seems to guarantee help for persons with roentgenographically discernible silicosis. The disease should not be permitted to develop so far." Later on in the book they say that the transfer of persons in occupations involving a high risk to dust-free or less dangerous work before signs of pulmonary disease have time to appear is only a last resort in prophylaxis against pneumoconiosis.

The other pneumoconioses, that is those covered by the Act of 1950, only yielded 36 notifications. These were 11 cases of asbestosis, 5 of talcosis, 5 of aluminosis, 8 of siderosis, 2 of berylliosis, 4 of hard-metal pneumoconiosis and 1 of anthracosis. These are presented in a similar fashion to the silicosis group.

The authors by their careful review of the material, have provided a sound basis for the extension of technical prophylactic measures. The only medical prophylactic measure they advocate is the examination of new entrants to jobs involving a risk of pneumoconiosis. The only compulsory medical examinations carried out at present are limited in practice to workplaces where it is feared disabling silicosis may occur. Stage 1 is not regarded as disabling. Until technical prophylaxis is perfected, the authors advocate a system of periodical examinations in all industries with a dust risk. This system is based on the gravity of the risk in different occupations as shown by their investigations. This scheme of suggested intervals for periodic medical examinations is worthy of consideration by all who have to do with pneumoconiosis.

This book provides easy reading for those familiar with the processes, and there is much information in its pages. The tables and diagrams are excellent. The reproductions of the radiological films are perhaps not always successful but they illustrate the conditions discussed very well. The book ranks as an excellent book of reference. *Charles L. Sutherland*

LÖBLICH, H. J. Elektronenmikroskopische Untersuchungen über die Entwicklung des Staubgranuloms. I. Befunde nach Applikation verschiedener Kieselgurformen. [**Electron Microscopic Investigation of the Development of Dust Granulomata. I. Findings following the Use of Various Forms of Kieselguhr**] *Beiträge z. Silikose-Forschung.* 1961, No. 71, 1–32, 15 figs. [47 refs.] II. Befunde nach Applikation von Quarz. [**II. Findings following the Use of Quartz**] *Ibid.*, 33–51, 7 figs. [25 refs.]

(I) This is a continuation of previous studies [Löblic *et al.*, this *Bulletin*, 1959, v. 34, 348]. 10 whit mice were given intraperitoneal injections of calcine and of flux-calcined kieselguhr. The animals wer killed at intervals of 7 days up to 35 weeks. Th method of preparing the sections is described. Prefe ence was given to the diamond for cutting section which were 400–600 Å thick. The electron micro scopic appearances of the granulomata after 7, 14, 2 to 35 days are given in detail with illustrations of eac of the stages. The essential features of these change in the first week are necrotic changes in the cells alon with the appearance of a homogeneous substance i the cytoplasm. In the granulomata arising from flux calcined kieselguhr, there is more connective tissu production, probably due to the presence of crysta line modifications in the injected material.

In this early stage, Phase I, the toxic action of bot forms of kieselguhr leads to cell destruction. After th second week, there is a proliferation of cells, Phase II in which there is an increased metabolism, which lead to an increase of fibrous tissue formation. After th first week the reaction to both forms of kieselguhr i essentially the same. The development of capillarie is discussed. The synthesis of collagenous fibrosis i considered to have an extracellular origin.

This electron microscopical study confirms that th early stages of granuloma production are non-specific the variations are only quantitative and do not sprin from any pathogenic difference. This holds good no only for the granulomata produced by the forms o kieselguhr but by those produced by other foreig bodies.

(II) This is a study of the early development o the quartz granuloma to shed light on the pathogeni action of various forms of silica. 20 albino rats wer injected with 50 mgm. quartz of a particle size 1·45 t 0·45 microns. The injection was made into an ai pocket produced by injecting 20 ccm. of air under th skin. The granulomata were removed from the ai pocket for electron microscopic examination at inter vals of 7, 14, 21 and 28 days. At the 7th day th granuloma has the same composition as young granula tion tissue. Cell walls are only partly retained. Th cytoplasm shows large vacuoles; these are prominen at each stage. The mitochondria are small. At th 14th day newly formed macrophages and some foreig body giant cells are seen; the cell walls are intact The mitochondria are intact. In the ground substanc fibrils appear. At the 21st and 28th day the mito chondria are swollen. Fibril bundles have increased i size. Quartz particles are found intracellularly. Afte the breakdown of the cells the particles appear indis tinct suggesting a covering of organic material on th surface. This is probably removed by the action o proteolytic ferments contained in the phagocytes whic engulf them. The contour of particles in intact cel is sharp.

The author disagrees with POLICARD *et al.* [th *Bulletin*, 1957, v. 32, 583] that there is a diminutio of the activity of quartz with time. He finds that a all stages the phagocytes are active. The activity o the phagocytes points to an increased metabolism du

to the action of quartz. The layer of protein on the surface of the quartz does not diminish its action. The development of fibrils sets in earlier and in greater amount in quartz granuloma than in the kieselguhr granuloma even where some silica is present.

The morphological changes offer no support to the immunity theory, they are evidence of a cytotoxic action. *Charles L. Sutherland*

LICHT, W. Experimentelle Untersuchungen zur Immunitätstheorie der Silikose. **[Experimental Tests of the Immunity Theory of Silicosis]** *Arch. f. Gewerbepath. u. Gewerbehyg.* 1960, v. 18, No. 3, 327–36, 2 figs. [15 refs.]

Three sets of experiments were made to ascertain if an antibody could be demonstrated in the serum of silicosis patients. In the first set of experiments the antigen was obtained from quartz particles of less than 5 microns, which were mixed with a protein obtained from a human lung by a process which is described in detail. This protein tested electrophoretically proved to be mostly serum albumin and gamma globulin. Controls were made from quartz particles and serum albumin and from quartz particles alone. The mixtures were incubated at 37°C. for 24 hours. The serum tested for agglutination were obtained from groups of 20 silicotic patients, 22 silicotuberculosis patients and from 26 women with no dust exposure. Some agglutination was found in all three groups; all groups showed more agglutination with protein-quartz than with quartz alone. The results are shown in a table and the conclusion is that the effects are non-specific.

In the second series the same material was used as in the first. The antigen and antibody were brought together by diffusion during an electrophoretic separation. The result should have been a fixing of the gamma globulin; there was, however, no definite diminution of the gamma globulin.

In the third series an attempt was made to use the possible presence of an antigen in silicotic hyaline substance, to prove the presence of an antibody in the serum of silicotic patients. If hyaline is the product of an antigen-antibody reaction, the antigen is already neutralized by the antibody. This however, may not be the case with glucoprotein. A polysaccharide extract was prepared and tested, along with an extract of serum albumin as control, to find if precipitation occurred with the serum of 30 silicotic patients and 30 healthy persons. Even after a long interval no precipitation occurred.

The author does not think that the negative results of his experiments entirely disprove the importance of immunity processes. Quartz and quartz with protein may not be suitable for provoking the formation of antibodies, and the silicosis antigen may well be of very different nature. VIGLIANI believes that the antigen is set free by the destruction of the macrophages; its origin appears to be bound up with the living cell and its metabolism [see also this *Bulletin*, 1961, v. 36, 1]. *Charles L. Sutherland*

GUYOTJEANNIN, C. & EYQUEM, A., with the technical collaboration of M. J. HOLEMANS, M. A. PALMIERI & J. ROBBA. Recherches immunologiques dans la silicose humaine. **[Immunological Studies on Silicosis in Man]** *Arch. Malad. Professionnelles.* Paris. 1960, Oct.–Nov., v. 21, Nos. 10/11, 635–42. [13 refs.]

Serological abnormalities in the blood of silicotic subjects were examined by two methods and the results compared. The agglutinin titres of the patients' sera were determined for (1) human red blood cells (group O) sensitized with an immune serum prepared in rabbits for human red blood cells (a modification of the Waaler-Rose reaction) and (2) polystyrene latex particles (0·81 μ diameter) coated with human globulin.

The Waaler-Rose reaction showed positive results in (1) 9 of 57 cases of uncomplicated silicosis, (2) 2 of 10 cases of tuberculo-silicosis, (3) 2 of 12 subjects in dusty occupations but without silicosis, (4) 132 of 243 with rheumatic diseases and (5) 1 of 18 controls. The latex agglutination test was positive in the corresponding groups as follows: (1) 8 of 56 subjects, (2) 1 of 10 subjects, (3) 1 (?) of 12 subjects. In 5 cases the latex agglutination reaction was strongly positive when the Waaler-Rose test was negative and in 8 the reverse was found. Other serological tests are described.

The results are said to confirm the existence of serological anomalies in some cases of silicosis but do not show whether the sole mechanism is an immunological one. *P. F. Holt*

STURM, W. Möglichkeiten der kardiopulmonalen Funktionsprüfung. **[Functional Tests of Heart and Lung]** *Ztschr. f.d.g. Hyg. u. ihre Grenzgebiete.* Berlin. 1961, Apr., v. 7, No. 4, 265–75, 1 fig. [Numerous refs.]

The English summary appended to the paper is as follows:—

"The report is a tabular summary of the frequently applied method of function testing of heart and lungs which is of special importance for the diagnosis and evaluation of professional silicosis diseases."

MÁNDI, A. Foglalkozási eredetü tüdömegbetegedésk elöfordulása a vas és fém, zománc és tüzállóanyagiparban. **[Occupational Lung Disease in the Iron, Metal, Enamel and Fireclay Industries]** *Munkavédelem.* Budapest. 1961, v. 7, Nos. 1/3, 37–41.

The author reviews present knowledge relating to silicosis, and in addition gives data of the frequency of silicosis in different Hungarian industrial branches, and, based on his own experiences, describes the radiological chest picture of enamel workers.

Examination showed that 4·9% of the iron and steel cleaners, 15·1% of the sand blasters and 18·1% of the

furnace bricklayers suffered from silicosis. The dust exposure is greatest in the fireclay industry [figures are not given] and it is not exceptional for workers aged 25–28 to be affected by serious silico-tuberculosis after a very short exposure.

The radiological chest examination of enamel workers has shown not only silicosis [FRIBERG and ÖHMAN, this *Bulletin*, 1957, v. 32, 766]. More often than in silicosis, the X-rays revealed, mainly in the lower lung fields, fine discrete and sharply defined granulation caused by the deposition of enamel dust. *Ladislaus Magos*

ROCHE, L., GALY, P., PASSERAT, M. & CANICAVE, J. Pneumopathies professionnelles chez les ouvriers travaillant dans une usine métallurgique de ferrochrome. [**Occupational Lung Disease in Workers Engaged in Crushing Ferrochrome**] *Arch. Malad. Professionnelles.* Paris. 1961, Jan.–Feb., v. 22, Nos. 1/2, 63–6, 5 figs.

4 cases of severe disabling pulmonary disease are described in men aged between 39 and 51 years who had been employed crushing ferrochrome at the same factory. The similarity of the symptoms, clinical findings, and occupational histories pointed conclusively to an occupational aetiology, although X-ray findings were not always typical. The disease was severe in all and rapidly progressive in 3: 2 men who had worked at the crusher for 5 years were totally disabled, the other 2 each with 7 years' exposure died. Unfortunately no autopsies were held.

X-ray findings indicated pulmonary fibrosis in all: in 2 there was miliary mottling with the later appearance of masses, in another there were opacities which were more suggestive of pulmonary tuberculosis than pneumoconiosis, and in the fourth true nodulation and masses were absent, the picture being described as diffuse bilateral fibrosis. All sputum examinations were negative for tubercle bacilli and antituberculous treatment did not help.

The ferrochrome was melted in an electric furnace and cast in ingot moulds in blocks weighing about 30 kgm. The ferrochrome contained only 3% quartz and 5 to 8% total silica. To facilitate removal of the castings, however, a bed of sand was placed at the bottom of the moulds. The air in the vicinity of the stamping and crushing machines contained 400 to 800 particles per cc. smaller than 3 μ of which 24 to 25% were quartz and cristobalite and 40% total silica.

From the clinical point of view these would appear to be cases of acute silicosis, but this is unlikely with such relatively low dust counts. The authors therefore suggest that the mixture of dusts has played a part and ask whether the association of chrome compounds with silica has not accelerated the development of these pulmonary lesions. They suggest that animal experiments would provide the answer. They note that none of the patients showed any signs of the usual effects of chrome such as dermatitis or rhinitis.

A. T. Doig

ROBERTSON, A. J., RIVERS, D., NAGELSCHMIDT, G. & DUNCUMB, P. **Stannosis: Benign Pneumoconiosis due to Tin Dioxide.** *Lancet.* 1961, May 20, 1089–93, 14 figs. (11 on pl.) [20 refs.]

ROBERTSON and WHITAKER reported in 1955 [this *Bulletin*, 1961, v. 36, 635] on radiographic abnormalities in 121 patients who had inhaled tin oxide dust or fume. These patients showed no decline of lung function with rising radiological category [GILSON, this *Bulletin*, 1960, v. 35, 1171]. Although the diagnosis of benign pneumoconiosis was probably correct there was no histological confirmation. The lungs of 7 of the patients have now been obtained and studied.

On macroscopical examination these lungs presented an appearance similar to that of the simple pneumoconiosis of coal workers. Histologically focal emphysema was not a prominent feature. Analysis of the dust in the lungs for tin oxide and silica was carried out. The amount of tin oxide varied from 0·5 gm. to 3·3 gm., and quartz from nil to 0·2 gm. These amounts of quartz were very small compared with those found in classical silicosis. To show that the dust in the phagocytes was tin, an X-ray-emission microanalysis was carried out by a procedure which is described. The presence of tin was confirmed. This method does not show that it was in the form of the dioxide but this had already been identified by the X-ray diffraction technique.

This tin ore comes from Bolivia and where it is mined cases of silicosis occur. In the concentrating plants the silica is washed out, and the workers there were shown to have similar appearances to the workers in Britain.

The authors consider that exposure to tin oxide of respirable size in sufficient quantity will give the diagnostic appearances whether the source be "fume" or "dust". The lungs of tin workers appear to contain about one-tenth the amount of dust found in coal workers. The higher atomic number of tin (50) makes it more easily seen radiographically than coal (6).

4 of the 7 deaths were due to coronary or cerebral thrombosis. No carcinoma or tuberculosis was reported. [ANSELL (*Lancet* 1961, v. 1, 1225) writes that he diagnosed stannosis in a patient in 1946. This patient, and 2 others he saw, died of carcinoma of the lung and he draws attention to a possible association. It will be remembered that a similar association has been claimed for siderosis.]

Charles L. Sutherland

MILENKOV, K., KIRIN, I., AGOPYAN, K. & ZAKHARIEVA, Z. [**The Effect of Hemp Dust on Certain Functions of the Body**] *Gigiena i Sanitariya* Moscow. 1961, v. 26, No. 4, 25–32, 8 figs. [In Russian.] English summary.

Workers in hemp factories in Bulgaria complained of fever, lasting a few hours or 2–3 days, and which affected new workers and to a lesser extent those returning from holiday.

The investigation of the character and development of the febrile reaction of the influence of the hemp dust on certain bodily functions was carried out on 2

volunteers who were put in the scutching part of the mill and on 2 newly joined workers. Also 102 factory workers in the most dusty parts were investigated. Animal experiments comprised the study of 15 rabbits in the scutching section and the study of aqueous and alcoholic extract of the hemp fibres on 6 rabbits and 12 rats. The clinical study included measurement of the temperature, arterial blood pressure (during Valsalva's manoeuvre) pulse, and various blood constituents—haemoglobin, erythrocytes, leucocytes (including phagocytic activity)—and with regard to the respiratory system: vital capacity, minute ventilation at rest, the minute consumption of oxygen, the FEV at 0·25, 0·5 and 0·75 and 1 second.

A description is given of the characteristic mill fever syndrome. The blood pressure (during Valsalva's manoeuvre, *i.e.* suporting a 40 mm. mercury column for 10 seconds) showed no abnormality. In the workers [presumably established workers] the arterial blood pressure shows changes corresponding to the extent of disturbance of pulmonary ventilation. Figures of tracings of arterial blood pressure show the slight increase at the time of the 3rd and 4th phases of the manoeuvre, in normal persons; a lesser degree of this and a less pronounced reflex bradycardia (of the fourth phase) in workers with obstructive type of ventilatory insufficiency; and finally, in the mixed type of ventilating insufficiency, the rise of the blood pressure in the third phase and bradycardia in the fourth are absent.

Changes in the haemoglobin, red cell count and ESR did not vary outside normal limits. The number of leucocytes rose during and just after the febrile reaction. this was an increase in polymorphs with a relative lymphocytosis. The phagocytic activity of the leucocytes was decreased in 20 (out of 24 volunteers) at the time of the febrile reaction, subsequently it rose.

In the volunteers the FEV fell after a 5–6-hour stay in the dusty atmosphere. Two cases are quoted; in one the one second FEV was 93% of the vital capacity before exposure and fell to 82%, in the other it fell from 87% to 75%. The 102 workers examined showed characteristic changes in pulmonary ventilation, and on the basis of these the cases were classified as obstructive, organic and mixed. 81 persons were put in the obstructive group, 12 in the mixed group, 2 in the organic group and 6 workers had normal lung ventilation [81+12+2+6=101 sic]. The 6 workers with normal lung ventilation were aged 20–30 years and all had about 5 years of work in the mill (apart from one with 13 years).

From the experimental results the point is made that although animals exposed to an atmosphere of the dust developed a febrile reaction similar to that seen in human subjects, there was no febrile reaction when aqueous and alcoholic extracts were injected into the animals. It is concluded, therefore, that stimulation of the respiratory tract is a necessary part of this neuroreflex and this, together with the absence of an eosinophilia, argues against an allergic basis.

It is suggested that the obstructive type of ventilatory insufficiency results from emphysematous changes together with the prolonged effect of hemp dust. The mixed type of ventilatory insufficiency is the result of byssinosis. *W. R. Lee*

Moreo, L. Rischio attuale di saturnismo nell'industria tipografica. [**Present Hazard of Lead Poisoning in the Printing Trade**] *Med. d. Lavoro.* 1961, Jan., v. 52, No. 1, 33–42. [20 refs.] English summary.

Type setting may be done by hand or by mechanical method in which whole lines are laid down at the same time, this being the linotype process. In the first method type made of an alloy of lead, antimony and tin is used, the smaller characters being the harder with a higher proportion of antimony. In the mechanical method a mixture having 85% of lead is used and the metal is kept hot so that it may be poured, line by line, into the matrix set up by the operator, where it at once solidifies. In addition to the procedures mentioned mechanical type setting with separate characters is also done (monotype process). Printing may be carried out by pressure on a flat or cylindrical surface and, alternatively, a sheet of alloy may be stamped out in the flat and transferred to a cylinder.

Though lead poisoning is much less common in the industry than it was early in the century the author decided to make a study of printing operatives, taking note of the excretion of protoporphyrin, coproporphyrin and basophil stippling of red cells. Protoporphyrin is found in the erythrocytes and was measured by spectrophotography; coproporphyrin is found in the urine and was estimated with the help of ultraviolet light. Tests for lead in the air, in dusts and in the blood, urine and on the hands of operatives were also made. The personnel worked in 5 different factories in the Milan area.

100 printing operatives were also seen when in hospital for various disorders and in these the blood picture was usually satisfactory, only 6 having too low a haemoglobin level. In 4 persons basophil stippling was seen and the erythrocyte protoporphyrin was within normal limits in all but 2 cases in which it was a little high. In all but 2 also the coproporphyrin in the urine was satisfactory. From 1941 to 1959, 127 compositors were sent to hospital for suspected saturnism. One was a woman who had to clean the type boxes frequently. She had slight hypochromic anaemia. Another patient had slight lead intoxication with symptoms and 5 had signs of lead absorption but no symptoms. It is felt that this hazard is now very small in Italian industry.

G. P. Pether

Horiuchi, K., Horiguchi, S., Nagano, Y., Hashimoto, K., Asano, I. & Noma, K. **A Survey on the Influence of Lead Exposure upon New Employees in an Electric Battery Work.** *Osaka City Med. J.* 1960, v. 6, No. 1, 71–7, 3 figs.

The survey lasted for 1 year on 4 groups of healthy men, aged about 20, who began work in rooms where the atmospheric concentrations of Pb in mgm. per m^3 were: 0·5—0·09; 0·3—0·5; 0·3; 0·5—1·8. Particle size of lead oxide dust was 0·2–3 microns. Average results of investigations are mostly presented in graph form. Values for controls, who were not exposed to Pb, were within normal limits and their blood counts improved during the year.

In the Pb groups red blood cells increased and haemoglobin decreased during the first month. After fluctuating for 2 months these curves settled lower than pre-exposure levels. No stippled cells were found beforehand and within 1 month every specimen had 1–7 per 10,000 red cells. Afterwards they were not found in all subjects. There was no significant reticulocytosis. Urinary Pb increased to peak values in 4 months, decreased slightly and remained at about 500-600 μgm. per litre, the 4 curves showing some correlation with atmospheric Pb concentrations. Faecal Pb values were similar. Urinary coproporphyrin excretion quickly increased. Average blood Pb concentrations increased slightly after 1 month, and after 6 months in the 4 rooms were : 58·8, 79·1, 72·2 and 60 μgm. per 100 gm. respectively; after 10 months the figures were 42·5, 39·8, 79·1 and 84. Before exposure these values were within normal limits, range 17·5-24·4. In subjects removed from exposure haemoglobin increased rapidly, urinary and blood Pb decreased, the latter gradually, and excretion of coproporphyrin diminished.

M. Patricia Fitzsimons

KNOP, W. Blei als Brandstifter. [**Fires in Accumulator Works Caused by Lead Dust**] *Zent. f. Arbeitsmed. u. Arbeitsschutz.* 1961, Apr., v. 11, No. 4, 84–6.

In this paper the author reports the occurrence of 2 fires in a lead accumulator factory. In both cases the filters installed to purify the dust-laden air were destroyed. Similar fires have occurred in other accumulator factories but their causation has not been accurately determined.

There is some account of the processes of lead accumulator manufacture in the course of which large amounts of a dust composed largely of lead oxide and finely divided metallic lead are produced. This dust is carried in ducts to the filter plant where it is filtered off by cotton filter cloths stretched on wooden frames. The explanation for the origin of the fires is that in dry weather—the fires occurred in January in successive years—when the winter air is dry—the filter cloths and the lead in the dusts lose moisture. Under these conditions the very finely divided metallic lead is more readily oxidized by atmospheric oxygen and by the oxygen given off by the lead oxide as the temperature rises. Ultimately the temperature becomes high enough to ignite the filters.

There is a discussion on methods for the prevention of these fires either by fireproofing the textile of the filters by treatment with chemicals which are mentioned or replacement of the present cotton material of the filters by metal mesh, nylon or other synthetic fibres, glass and asbestos. Mention is also made of the possibility of bringing about the deposition of the lead dust by centrifugal methods. *M. E. Delafield*

PORTAL, R. W. **Cerebral Tumour in a Lead Worker.** *Brit. J. Indust. Med.* 1961, Apr., v. 18, No. 2, 153–6.

Lead encephalopathy was the initial diagnosis and the discussion shows why this was unlikely. A previously healthy man, aged 63, after brief unconsciousness, was irritable, had unequal pupils, his left arm was immobile; he could not speak and he had a petechial rash. He was in good health up to the night of his admission and all abnormal neurological signs disappeared by the following morning. Confusion and pyrexia appeared for 5 days and 2 epileptiform attacks with weakness of the left side. Meantime investigations showed only proteinuria and 6,000-12,000 stippled cells per million red cells. Details of EDTA infusions are given in the table below. After the first infusion early in January, blood Pb was 190 mgm. per 100 ml. The patient, apparently recovered, was at work before the February infusions.

In April his condition deteriorated, with headache, personality changes, obesity and left facial palsy with hemiparesis. Electroencephalopathy—and lumbar puncture, both previously normal—now indicated a right fronto-temporal space-occupying lesion, confirmed by carotid angiography which had not been done before. The patient died 4 weeks after admission, and post-mortem examination showed a frontal astrocytoma and, otherwise only microscopic regenerating renal tubular changes. The Pb contents in μgm. per gm. wet tissue were: skull 170; femur 120 (the upper limit of normal ranges and presumably lowered by the EDTA); kidney, medulla 2, cortex 2·9; heart 0·4. The schedule of EDTA was as follows:

Date		EDTA	Urinary lead in mgm. per 24 hours	per litre
Jan. 4	...	1 gm.	3·78	1·18
5	...	—	0·38	0·42
7	...	1 gm.	2·75	1·25
8	...	2 gm.	2·88	1·10
Feb. 18	...	—	0·036	0·02
19	...	2 gm.	2·22	1·0
20	...	2 gm.	1·45	0·72

Pb poisoning had been notified because of: the coarse stippling; previous positive porphyrinuria tests; recent shovelling of litharge while the patient had a cold; EDTA response. The normal EDTA response is 0·22-0·65 mgm. Pb per 24 hours. However, the patient had worked with Pb for 35 years, had absorbed excess Pb, but had no colic or anaemia, indicating that he was not susceptible to poisoning. The notification was withdrawn.

Pb compounds were once used for treating neoplasms, though not for primary cerebral tumours, because Pb is cytotoxic. The absorbed Pb is therefore unlikely to have accelerated growth of the tumour, but whether it rendered this patient more liable to epilepsy is a matter for speculation. [See, for contrast, this *Bulletin*, 1961, v. 36, 637.] *M. Patricia Fitzsimons*

KIRCHER, RITTER, J., MARTI, FECED & BELAOUANE. Fréquence des lésions corticales dans le manganisme. Projet de bâreme d'invalidité. [**Frequency of Cortical Lesions in Manganese Poisoning: Scheme of Rates of Disability**] *Arch. Malad. Professionnelles.* Paris. 1960, Dec., v. 21, No. 12, 736–42, 5 figs. Discussion 742–3.

The neurological signs of manganese poisoning are described and the localization of the lesions is discussed.

Autopsies on victims of this poisoning are rare and information can only be obtained from clinical and experimental evidence, from the results of surgery and the effects of trauma. Modern research shows that the lesions are more likely to be found in the frontal lobes than in the basal ganglia or even the cerebellum. Pneumoencephalograph examinations were made by the authors in 10 cases and 5 photographs illustrating the findings are given. The ventricles were normal in size and position. Symmetrical cortical damage of the prefrontal region was constantly found. No lesions were found in the posterior region. A scheme of rates of disability is given for the 4 stages of the disease. The initial stage presents subjective symptoms such as anorexia, cramps, drowsiness and changes in behaviour. At this stage the worker changes his job to protect himself and to allow detoxication. The intermediate stage covers the onset of objective signs, such as speech difficulties. the mask-like facies, retropulsion without falling, slow clumsy movements, sweating and sialorrhoea. The job is changed and a disability rate of 1 to 20 per 100 proposed.

The established stages is that of the appearance of muscular hypertonus in extension and the award proposed for the group is 20 to 70 per 100. Separate assessments are given for individual signs such as tremors, local in upper limbs, diffuse in lower limbs (10 to 20 per 100) and *pas du coq*, retropulsion with falling, no Rombergism (60 to 70 per 100).

The stage of permanent deformity has a proposed rate of 70 to 100 per 100, and again separate assessments are proposed for different effects, such as chronic torticollis 15 to 20 per 100 and upper limb deformity 75 per 100. Manganese pneumonia has not been seen by the authors but if it should occur they would give for the resultant pleural conditions the rate given for such conditions following thoracic trauma. In the discussion on this paper M. L. DÉROBERT raised objections to the proposed scheme of rates. The tendency would be to add up the rates for different signs. The victim of psychic disorders (40 per 100) along with speech difficulty (10 to 30 per 100) would have a maximum rate of 70 per 100 which would be too high. The rate should be judged by the total disability produced by the poisoning and not by individual signs taken separately. He objected further to any rigid set of rates being laid down at all. One cannot put medicine or biology into the rigid framework of an algebraic formula. *Charles L. Sutherland*

HATEM, S. Essai sur le mécanisme de la cancérisation par les métaux. Le rôle de l'histamine et la prophylaxie par EDTA. [**Mechanism of Cancer Induction by Metals. Role of Histamine and Prophylaxis by EDTA**] *Arch. Malad. Professionnelles.* Paris. 1961, Jan.–Feb., v. 22, Nos. 1/2, 40–46, 5 figs. [51 refs.]

Cancers can be produced experimentally by nickel, cobalt, chromium, beryllium and silver, and occupational exposure to several of these metals has produced cancer in man. All the metals have an affinity for histamine and form a complex with it. Some of them will displace calcium from the calcium disodium salt of ethylene diamine tetra acetic acid [EDTA] and this salt has been used in the treatment of metal poisoning. The salt will prevent the carcinogenic effect of nickel and beryllium, but not of cobalt [this *Bulletin*, 1953, v. 28, 956, 1063]. The present study was conducted to see whether the salt would destroy the metal-histamine complex. It was found to do so in the case of nickel and beryllium, but not in the case of cobalt. It is concluded that these results support the hypothesis that histamine block facilitates the development of cancer. *Richard Doll*

MAGISTRETTI, M. & PEIRONE, E. **The Action of Carbon Disulphide on Cerebral Monoamine Oxidase.** *Med. d. Lavoro.* 1961, Jan., v. 52, No. 1, 1–10, 4 figs. [Numerous refs.]

Recent experiments have shown that serotonin or 5-hydroxytryptamine plays an essential part in certain functions of the central nervous system. Certain investigators suggest that the sedative action of reserpine is related to the amount of serotonin in the brain, the first step in the breakdown of which is an oxidative deamination by monoamine oxidase. If an inhibitor of this oxidase, such as iproniazid, is exhibited reserpine causes excitation rather than sedation. It has been shown that CS_2 reacts with various substances having SH groups and the authors have shown experimentally that CS_2 can inhibit monoamine oxidase both *in vivo* and *in vitro* and in the brain this is associated with a rise in free serotonin. It is thought therefore that this provides some evidence of the nature of CS_2 poisoning. Rats seem more sensitive to this substance than human beings. In the experiments here described the authors related the inhibition of monoamine oxidase to the rate of disappearance of 5-hydroxytryptamine incubated with rat brain material. Recovery from the effects of CS_2 in rat experiments seems to be prolonged as these proceed and it is likely that the intervals between tests were too short to enable the inactivated monoamine oxidase to recover its functions fully. CS_2 will react with thioglycolic acid, potassium thioglycolate, methyl glycine, BAL, cysteine and glutathione and there is a significant reduction of SH groups in the blood of workers exposed to it but between exposures, recovery is fairly rapid. *G. C. Pether*

NOFER, J., CHOJNOWSKI, J., KAWECKA, M., KIEC, E., WRONSKA-SZPAKOWA, T. & WYSZOMIRSKA, Z. Wpływ zawodowego narażenia na dwusiarczek wegla na powstawanie miażdżycy. [**Effect of Occupational Hazard to Carbon Disulphide on the Pathogenesis of Arteriosclerosis**] *Med. Pracy.* 1961, v. 12, No. 2, 101–18, 5 figs. [20 refs.]

The English summary appended to the paper is as follows:—

"103 workers (males) exposed to the action of CS_2 in the viscose fibre plant and 79 workers (males) having

no contact with the CS_2 were examined. The age in both groups was identical. In workers exposed to CS_2 were stated statistically significant more frequent vascular changes in retina, coronary changes in the electrocardiograms, higher systolic pressure and more frequent changes after effort test in comparison with the control group. In the same time in workers of viscose fibre plant higher average contents of cholesterol and of phospholipids in blood serum were stated. A higher value of the relation of beta lipoproteins to alpha proteins was also found. In this group when compared with the control one the increase of the relation of cholesterol to phospholipids and of the relation of total cholesterol to the free one was also stated. The total serum protein level was higher in the exposed group.

"The authors' opinion is that these results, obtained in persons in whom no clinical symptoms of intoxications were found, prove that only a long-term exposure to CS_2 provokes disturbances in the vascular system and in the metabolism of lipids which are very similar to those found in the arteriosclerosis."

Wronska-Szpakowa, Teresa, Liniecki, J. & Brykalski, D. Wpływ CS_2 na zachowanie sie podanego jednorazowo radioaktywnego cynku. Doniesienie wstepne. **[Effect of CS_2 on the Behaviour of the Single Dose of Radioactive Zinc. (Preliminary Report)]** *Med. Pracy.* 1961, v. 12, No. 2, 119–23, 2 figs.

The English summary appended to the paper is as follows:—

"The experiment was made in order to study the effect of CS_2 intoxication on the zinc metabolism.

"A single dose of 40 μg of Zn^{65} in the form of ZnC_2 was given to albino rats, divided into two groups, each containing 6 animals. One of these groups was intoxicated with CS_2 during the 30 days before Zn^{65} administration: every day 0·2 ml/kg of CS_2 was injected subcutaneously. During 4 days the determination in urine and faeces were made, then the animals were killed and the zinc content in blood and different organs was determined. The obtained results show that in animals intoxicated with CS_2 the elimination of Zn^{65} in urine and faeces decreases about twice. In the same time in intoxicated animals the Z^{65} content increases in the organs, especially in liver, kidneys and heart. In blood and spleen of the animals in the intoxicated group Zn^{65} content is lower in comparison to controls."

Wronowa, Barbara. Wpływ CS_2 na wydalanie kwasu nikotynowego i tzw. całkowitego kwasu nikotynowego u świnek morskich. **[Effect of CS_2 on the Elimination of Nicotinic Acid and so called Total Nicotinic Acid in Guineapigs]** *Med. Pracy.* 1961, v. 12, No. 2, 125–8. [11 refs.]

The English summary appended to the paper is as follows:—

"In relation with opinions of other authors who have stated some disturbances in the elimination of metabolites of thiamine and with data proving the protective action of vitamin PP in the course of carbon disulphide intoxication, the attempts were made to explain some problems connected with the metabolism of nicotinic acid. For this purpose the studies were carried out on guinea pigs exposed during the experimental period of 9 months to the action of CS_2 in the concentration of 1·5 mg/l of air. One group of animals was given nicotinic acid in a daily dose of 25 mg. In the urine of exposed and control animals determinations of nicotinic acid and of total nicotinic acid were made using the modified König's method. The diet of exposed and control animals was fixed and contained from 0·4 to 0·6 mg. of nicotinic acid in the food given to each animal per day.

"On the basis of investigations it was stated that the elimination of nicotinic acid in animals exposed to CS_2 is significantly lower (about 3.4-fold) when compared with control groups."

Knobloch, Krystyna. Zmiany chronaksji przedsionkowej i ruchowej u świnek morskich w przewlekłym zatruciu dwusiarczkiem wegla. **[Changes in Vestibular and Motor Chronaxy in Guineapigs intoxicated chronically by Carbon Disulphide]** *Med. Pracy.* 1961, v. 12, No. 2, 129–37, 4 figs. [10 refs.]

The English summary appended to the paper is as follows:—

"12 male guinea pigs were used in the experiment made in two series. In the first, 6 animals were intoxicated: 3 of them were exposed to the action of CS_2 in concentration 1·44 $\mp$ 0·16 mg/l of air, the other 3 were exposed to the action of CS_2 vapours in concentration 0·79 $\mp$ 0·16 mg/l of air. The experiment lasted for 6 days weekly up to the death of the animals (39 weeks).

"In both groups the changes of vestibular chronaxy were similar and had phasic character. In the first phase the shortening of chronaxy (excitability increase) was stated, the second phase was characterized by a slow chronaxy increase (excitability decrease), in the third phase the stability of increased chronaxy was observed and in the fourth phase the chronaxy decrease, which before death had general values lower than initial ones, was observed.

"In the course of changes of motor chronaxy only the phase of chronaxy decrease tending to shortening in the period preceding the death of animal was observed.

"In the second series of experiments 6 animals were used. They were submitted to the action of CS_2 vapours in concentration 0·82 $\mp$ 0·06 mg/l of air in the same manner as in the first series. It was stated that the decrease and the increase of chronaxy of the eyeball deviation reflex as well as of flexion and extension of the anterior limb fingers is statistically significant, the probability being greater than 99%.

"Moreover, the significance of chronaxy decrease for the head inclination was also proved with the probability greater than 95%."

BRIEGER, H. **Chronic Carbon Disulfide Poisoning.** *J. Occup. Med.* Chicago. 1961, June, v. 3, No. 6, 302–8. [90 refs.]

SCIARINI, L. J. & MEIGS, J. W. **The Biotransformation of Benzidine. II. Studies in Mouse and Man.** *Arch. Environment. Health.* Chicago. 1961, Apr., v. 2, No. 4, 423–8. [10 refs.]

Previous studies [this *Bulletin*, 1959, v. 34, 770] were extended to mice because of the limited ability of dogs, in contrast with man, to acetylate aromatic amino groups. Of 9 probable excretion products, 7 were found in the urine—including acetyl, sulphuric ester and glucuronic acid derivatives. Tables present quantitative and calculated recoveries after analysis by 2 methods. The total recovery was 12 mgm., as benzidine, of the 80 mgm. injected intraperitoneally into 20 mice (100 mgm. benzidine, suspended in tragacanth, per kgm.). This was in 38 ml. urine collected in the first 24 hours after injection; other specimens were also collected.

The results give a basis for urine analysis in men engaged in the manufacture of benzidine. The chemical procedures were adapted to lower concentrations expected where skin absorption was guarded against particularly by full sets of clean working clothing. Urine was collected for 5 days from 2 groups at the end of the day's work in March and August, when the plant was used exclusively for benzidine manufacture. Mean concentrations of benzidine were respectively 0·23 and 0·674 mgm. per litre. Metabolites were analysed in 4 individual samples which contained the highest concentration. A table gives these figures, and the mean values, expressed as mgm. of benzidine per litre, in March and August respectively were: benzidine 0·28 and 0·79; monoacetyl benzidine 0·27 and 0·36; diacetyl benzidine 0·52 and 1·12; 3 hydroxy-benzidine 3·9 and 19·6; and the total mean recovery 4·99 and 21·82.

In the mice the proportional distribution of recoveries was: benzidine 10%; mono- and di-acetylbenzidine 3·4% and 2·6%; and the following derivatives of benzidine, 3-OH ethereal sulphate 29%, monoacetylated 3-OH ethereal sulphate or glucuronide or both 25%, N-hydrogen sulphate or glucuronide or both 18% and 3-OH glucuronide 12%. *M. Patricia Fitzsimons*

SALMOWA, Jadwiga. Ilościowa ocena wchłaniania nitrobenzenu. II. P-nitrofenol jako metabolit nitrobenzenu w niskim zakresie dawek. [**Quantitative Evaluation of Nitrobenzene Absorption. II. P-Nitrophenol as Metabolite of Nitrobenzene in the Low Range of Absorbed Doses**] *Med. Pracy.* 1961, v. 12, No. 2, 145–55, 4 figs. [10 refs.]

The English summary appended to the paper is as follows:—

"This paper is a continuation of the attempt to find out a nitrobenzene metabolite which could serve as an absorption index of this compound.

"On the basis of preliminary experiments it was shown that the p-aminophenol cannot be used as an absorption index, chiefly because of its presence in urine of non exposed persons and of the low efficiency of excretion when small doses are absorbed. In this study attention was put on the other nitrobenzene metabolite—the p-nitrophenol, which was determined in urine by means of own modification of Lawford's and Harvey's and Vlachova's methods.

"Experiments were carried out on rabbits and rats to which nitrobenzene in doses of 0·5 to 100 mg/kg was given intravenously. The results of experiments have shown, that the efficiency of elimination of p-nitrophenol in the urine of animals is significantly higher than this of p-aminophenol elimination. It is especially pointed out when the nitrobenzene doses are small (0·5 mg/kg) and the efficiency of p-nitrophenol elimination amounts to 50%, whereas the p-aminophenol determination after administration of doses even ten-fold higher (5 mg/kg) was not possible.

"The p-nitrophenol and p-aminophenol determinations were also made in workers exposed to the nitrobenzene absorption. The obtained data confirm the adequacy of application of p-nitrophenol test.

"Further investigations on dependence between absorbed doses of nitrobenzene and the amount of p-nitrophenol eliminated in human urine are continued."

[For part I see this *Bulletin*, 1960, v. 35, 547].

LEMBECK, R. Einige Vorschläge zur Verbesserung der Technik zur Bestimmung der Brechungsindizes nach der Immersionsmethode. [**Improvements in the Immersion Method for Determining Refractive Index**] *Staub.* Düsseldorf. 1961, Apr. 1, v. 21, No. 4, 183–6, 5 figs.

The toxicity of the vapours of a number of liquids employed in microscopy is indicated and some non-toxic substances are listed with their refractive indices and dispersive powers. When toxic liquids are used for the identification of particles by the immersion method, particularly with a heated stage, it is advisable that air be exhausted above the stage so that the observer cannot inhale fumes.

Difficulty may arise with a heated stage owing to the temperature of the immersion liquid being below that of the stage, which causes an error in refractive index. A heating device, operated with warm air, is described which ensures that the temperature of the liquid is known accurately. *C. N. Davies*

BREYSSE, P. A. **Plastics in Automobile Body Repair Shops.** *Indust. Med. & Surgery.* Miami. 1961, Apr., v. 30, No. 4, 141–4.

Polyester and epoxy resin systems are being used for motor-car repairs. Their use involves potential fire and health hazards and workers should be trained in methods of prevention and protection. Face shields, dust respirators, gloves with disposable linings, aprons, covered waste receptacles, local exhaust ventilation and washing facilities are needed. Where large quantities of the resins are used it is preferable to isolate this work from the general workshop, and if both resins are

used operations with each should be kept separate to avoid accidental mixing of the epoxy resin amine hardener with the methyl ethyl ketone peroxide from the polyester resin. Repair processes include preparation of the plastic, application, curing—usually at room temperature—finishing by sanding or grinding, and painting. The health hazards are skin or eye contact with irritants, dermatitis or other sensitization disorders, and illness or lung damage from inhalation of vapour or dust. Much of the dust produced during finishing is from the filler materials. These may be pulverized wood, shell, soya bean, nylon fibre or silica flour, asbestos, mica, antimony trioxide or fibre glass. The possibility of ignition of air-borne dust is a matter for concern.

With polyester resins the main risk is from fire or explosion. Styrene is a major constituent, and the catalyst is an organic peroxide: organic peroxides can burn even when smothered with carbon dioxide. Shocks, friction, heating and the presence of volatile solvents with low flash points should be guarded against.

With epoxy resins the curing temperature depends on the particular resin involved and the characteristics desired. The article includes a 2-page copy of the Boeing Airplane Company's hazard control bulletin which contains lists of the various materials used and the hazardous properties of those which have been investigated. [See this *Bulletin,* 1961, v. 36, 538, 539, 540.] *M. Patricia Fitzsimons*

TOLOT, F., COLIN, M. & SOUBRIER, R. Asthme et araldite. [**Asthma and Araldite**] *Arch. Malad. Professionnelles.* Paris. 1961, Mar., v. 22, No. 3, 163–4.

Attacks of asthmatic dyspnoea appeared in a man aged 60 after 1 month's exposure to dust and vapour in a workshop where araldite insulators were manufactured. He had been in good health, with no respiratory disease except acute bronchitis once 40 years previously, even though from 1943 to 1953 he had worked where there was a silicosis risk. X-ray examination of the chest showed simple reticulation and no nodulation. The *histamino-pexique* power of the serum was practically nil. Patch tests were weakly positive to the resin and strongly so to the hardener. There was no handling of the resin as is the case when dermatitis has been reported from epoxy resins. In this workshop dust arose during moulding and turning and vapour of the hardener was evolved during heat curing. This illness shows the need for scrupulous preventive measures. Though the patient was probably an allergic subject, his negative past history added to the reasons for incriminating araldite as responsible for the respiratory symptoms. *M. Patricia Fitzsimons*

CÉLICE, J. & FOURNEL, J. Emploi d'un réactivateur des cholinestérases (le sulfométhylate de l'α-pyridylaldoxime 7676 RP), dans les intoxications expérimentales par les insecticides organophosphorés. [**The Use of a Cholinesterase Reactivator in Experimental Poisoning by Organophosphorus Insecticides**] *Arch. Malad. Professionnelles.* Paris. 1961, Mar., v. 22, No. 3, 101–7. [19 refs.]

A comparison has been undertaken to test the efficiency of pyridine-2-aldoxime methosulphate (7676 RP) with pyridine-2-aldoxime methiodide (PAM) in protecting animals poisoned with organophosphorus compounds.

Compound 7676 RP does not cause renal lesions. Its properties are virtually identical to those of PAM but it is more water soluble. It is equally as active as PAM in reducing the mortality rate of mice poisoned with parathion and also in the degree of reactivation of inhibited cholinesterase activity of serum from rabbits poisoned with parathion. Compound 7676 RP was found to be an effective antidote against parathion (diethyl 4-nitrophenol phosphorothionate), endothion (2-[dimethoxyphosphinylthio]methyl-5-methoxy-4-pyrone), demeton-O (diethyl 2-ethylthioethyl phosphorothionate) and demeton-methyl and ethion (bis[diethoxylphosphinothioylthio]methane) but not against sevin (α-napthyl N-methylcarbamate). In selected doses compound 7676 RP in conjunction with either atropine or isothazine gave complete protection to mice against parathion. When given to rabbits, together with atropine, it tended to increase the toxicity of parathion in the doses used. *J. E. Cremer*

CÉLICE, J., FOURNEL, J., HILLION, P., BARTHELMÉ, P. & ROGER, S. Traitement des intoxications humaines dues aux dérivés organophosphorés par les méthodes classiques et le sulfométhylate de l'α-pyridylaldoxcine (7676 RP). [**The Treatment of Organophosphorus Poisoning in Man by Classical Methods and with Pyridine-2-Aldoxime Methosulphate**] *Arch. Malad. Professionnelles.* Paris. 1961, Mar., v. 22, No. 3, 108–19. [12 refs.]

4 cases of parathion (diethyl 4-nitrophenyl phosphorothionate) poisoning and 2 suffering from endothion (2-[dimethoxyphosphinylthio]methyl-5-methoxy-4-pyrone) poisoning are fully described together with the earlier recommended treatment which combined the use of atropine sulphate and diparcol. 3 further cases of parathion poisoning are reported in which a new compound, pyridine-2-aldoxime methosulphate (7676 RP), was used successfully in conjunction with atropine. The compound 7676 RP is closely related to PAM (pyridine-2-aldoxime methiodide). Both compounds reverse the inhibition of cholinesterase by certain organophosphorus compounds and their therapeutic use is considered valuable in cases of poisoning. Details of a new general scheme of treatment are given which include the immediate administration of atropine, diparcol and pyridine-2-aldoxime methosulphate. The authors stress that morphine or theopylline should never be given. *J. E. Cremer*

HOBBIGER, F. **The Inhibition of Acetylcholinesterase by Organophosphorus Compounds and its Reversal.** *Proc. Roy. Soc. Med.* 1961, May, v. 54, No. 5, 403–5 (Sect. Comp. Med. 9–11). [17 refs.]

LADELL, W. S. S. **Physiological and Clinical Effects of Organophosphorus Compounds.** *Proc. Roy. Soc. Med.* 1961, May, v. 54, No. 5, 405–6 (Sect. Comp. Med. 11–12).

LE MOAN, G. Intoxications par les pesticides. Étude chimique et toxicologique. **[Poisoning by Pesticides. Chemical and Toxicological Studies]** *Arch. Malad. Professionnelles.* Paris. 1961, Apr.–May, v. 22, Nos. 4/5, 226–42. [12 refs.]

This is the opening paper in a symposium on the hazards of pesticides. After briefly discussing the ways in which poisoning by pesticides can occur, the need for their full toxicological investigation and the analytical techniques required for their estimation the author discusses the properties of the pesticides in common use in agriculture. The groups mainly discussed are the organic chlorine compounds, the organo-phosphorus compounds and the organo-mercurials.

[The bibliography is restricted to review articles and books.] *H. B. Stoner*

CÉLICE, J. Étude clinique et traitement de quelques intoxications par les pesticides. **[Clinical Features and Treatment of Poisoning by Certain Pesticides]** *Arch. Malad. Professionnelles.* Paris. 1961, Apr.–May, v. 22, Nos. 4/5, 243–60.

The author discusses the symptoms, prophylaxis and treatment of poisoning by the following insecticides and fungicides: methyl bromide, chloropicrin, ethylene oxide, carbon tetrachloride, tetrachlorethane, trichloroethylene, p- and o-dichlorobenzene, DDT, hexachlorocyclohexane [benzene hexachloride], dieldrin, chlordane, heptochlor, hexachlorobenzene, toxaphene, dinitrocompounds, nicotine, organo-mercurial compounds, thiram, ziram, dodine, kerosene and organo-phosphorus compounds. After describing in detail the usual treatment of poisoning by these substances, particularly by organo-phosphorus compounds, he discusses the general therapeutic measures which are applicable to these cases. The author describes his experimental and clinical experience with the reactivating agent 7676 RP, the sulphomethylate of pyridine 2-aldoxime. It is emphasized that reactivating agents are not effective against all organo-phosphorus compounds, a notable exception being sevin. *H. B. Stoner*

VACHER, J. Le diagnostic des intoxications par les pesticides. **[The Diagnoses of Poisoning by Pesticides]** *Arch. Malad. Professionnelles.* Paris. 1961, Apr.–May, v. 22, Nos. 4/5, 260–65.

The author describes the ways in which poisoning by pesticides can occur and the steps in the clinical diagnosis of such cases. Particular attention is paid to the taking of the history of the case and the type of information required to establish a case of poisoning by pesticide is discussed. With the rapidly increasing number and types of pesticide and with their widening use steps should be taken to make the information about them readily available to the non-specialist doctor confronted with a case of poisoning. One solution is the setting up of "poison centres" similar to those in Paris and Lyons. This is an effective method for more densely populated areas but less so in rural areas. Consequently he considers it essential to set up a central reference bureau for the dissemination of information in response to telephone calls. While this would at first be on a national basis a similar international information bureau would ensure that therapeutic advances would quickly become widely known. As an example of this he cites the extensive Japanese experience in using reactivating agents in the treatment of organo-phosphorus poisoning.

H. B. Stoner

KRISHNAMURTHY, K., KRISHNAKUMARI, M. K. & MAJUMDER, S. K. **Studies on the Oral Toxicity and Metabolism of Citicide in Albino Rats.** *Ann. Biochem. & Exper. Med.* Calcutta. 1960, Dec., v. 20, No. 12, 333–40. [16 refs.]

Citicide described as "a polychloro derivative of turpentine" and related to toxaphene and chlorinated camphene has shown promise as an insecticide against a variety of pests.

A single dose of 6 gm. per kgm. by mouth to albino rats killed only 2 out of 30. The rats displayed hypersensitivity for about 3 days. Reference is given to a colorimetric method for estimating citicide.

The food intake, citicide excretion, and urinary chloride (total, inorganic and, by difference, organic); ethereal sulphate; glucuronic acid and mercapturic acid were recorded for over 5 days in 6 rats given 6 gm. per kgm. of citicide. Of the dose given 16–38% of the citicide was excreted unchanged. Ethereal sulphate and glucuronic acid excretion was high in the first 3 days indicating a rapid metabolism of the citicide that had been absorbed. The body fat did contain some organic chloride but the specific test for citicide was negative indicating that it was a metabolite that was laid down in fat. Only mild cellular changes were seen in the livers and kidneys of rats killed 5 days after citicide.

J. M. Barnes

AWAAD, H., EL-SHERBINI, A. F., HAMMOUD, E., HAZAA, I., KHARADLY, M. & VALIC, F. **Radiation Hazards in Red Sea Phosphate Mines.** *J. Egyptian Pub. Health Ass.* 1961, v. 36, Nos. 1/2, 1–14. [22 refs.]

A geophysical team of the Atomic Energy Commission of the United Arab Republic having reported that some areas on the Red Sea Coast had a level of background radiation averaging up to 10 times the normal for the country, the authors selected 4 mines for preliminary work, 2 in Kosseir and 2 in Port Safaga, to find the radiation levels, especially that due to radioactive dust, and to try to assess the effects upon the working personnel. The data relating to 3 of the mines

are given in Table 2 which show that 2 of the mines had a concentration, given in $\mu\mu$curies per litre of air, roughly 10 times as high as that of the other.

The results, compared with the most conservative of the quoted (p. 5) recommended maximum premissive level, show concentrations (listed in Table 2) ranging from 3·6 to 89·7 times the maximum allowed. Clinical and laboratory examinations of the 292 male workers were carried out. The results were entirely reassuring for no pathological changes due to irradiation could be proved. In spite of this, the authors of this excellent record recommend better ventilation of the mines and systematic medical inspections. *S. Russ*

Abrahams, A. P., Carmichael, P. & Kleinfeld, M. **A Study of Occupational Radiation Exposure in New York State.** *Amer. Indust. Hyg. Ass. J.* 1961, Apr., v. 22, No. 2, 124–9, 5 figs.

Industrial Code Rule 38, entitled Radiation Protection has been in use in N.Y. State since December 1955. The responsibility for the administration and enforcement of this Code lies with the Division of Industrial Hygiene of the Department of Labour.

In 1960 a study was initiated in order to determine:— (1) The degree of radiation exposure by occupation, source and industry. (2) The relationship between dosimetric and survey measurements. (3) The contribution of occupational exposure to total population dose. (4) Whether industry can readily comply with the lower dose limits proposed in a revision of the State Code.

It was found that over 90% of the exposures were below the National Committee on Radiation Protection recommended dose limit of 100 mrem per week, and that the contribution of occupational exposure to the general population dose was less than 0·3%. The highest external exposures noted were among workers in radium processing, luminous dial painting, industrial radiography and nuclear fuel element fabrication.

The conclusions drawn from this survey are generally reassuring and the numbers of people examined were significant; the monitoring data were obtained from nearly 2,500 employees and the four main questions posed could be answered with some confidence. The occupational exposures to radiation were below 50 mrem per week in at least 90% of the radiation workers; there was close agreement between dosimetric and survey measuremnts. The contribution of the exposures to the general population dose is a small fraction of that due to medical and other environmental sources. *S. Russ*

Selby, J. M., Bowen, B. M. & Edgerton, J. H. **Environmental Monitoring at Georgia Nuclear Laboratories—AFP 67.** *Amer. Indust. Hyg. Ass. J.* 1961, Apr., v. 22, No. 2, 114–18, 5 figs.

This article is not concerned with safety measures for the personnel at work upon reactors, but with a special study of environmental features. The operation of a reactor creates many safety problems; one is how to deal with the release of solid liquid or gaseous radioactive materials to the environment.

A monitoring programme was initiated in 1957 to provide basic background data on radioactivity density found in ground and surface water, soil and vegetation. To meet operating requirements the programme has been expanded to include the collection and measurement of air, soil, water, vegetation, mud and wild life samples.

The article is illustrated by excellent diagrams and could well serve as a model to those who have the onus of safety in any big radiation undertaking. In the present instance about 1,000 measurements are made monthly to maintain a comprehensive picture of radiation levels from "naturally" occurring isotopes and plant operation.

It is stated that to date no significant contamination or radiation levels have been detected except in the area immediately surrounding the reactor and the maximum permissible concentrations established by Federal Regulations have not been exceeded in the environs inhabited by controlled or un-controlled personnel. *S. Russ*

Bonta, J. & Voit, E. A sugárvédelem néhány szervezési kérdése. **[Organization for the Prevention of Radiation in Hungary]** *Munkavédelem.* Budapest. 1961, v. 7, Nos. 1/3, 33–7.

The Department of Occupational Health of the Ministry of Health is the main directing and controlling organization for the prevention of radiation in Hungary. An isotope laboratory can get isotope materials only by permission of the Ministry of Health, and this permission is given after scrupulous health examination of the laboratory. To secure suitable conditions for isotope work, new isotope laboratories can be planned by one specialized firm. Directed by the Ministry, the Department of Radiation Hygiene of the Institute of Occupational Health carries out not only research but also practical work, the most important of which is to control isotope and industrial laboratories in the whole country, except the capital. In Budapest this work is done by the Radiation Safety Unit of the Public Health and Epidemiological Station. *Ladislaus Magos*

Hoover, R. L. **Industrial Hygiene Techniques in the Decontamination of a Building contaminated with Radium.** *Amer. Indust. Hyg. Ass. J.* 1961, Apr., v. 22, No. 2, 83–5.

This is a study on radioactive contamination on a fairly big scale; a 5-storey building which has been in use for about 50 years, during which time radium work of various technical kinds (not medical) was carried out. The whole building was found to be contaminated and an initial survey in some of the rooms indicated a general radiation flux ranging from 5 to 500 mrem per hour. Most of the contamination was well into floors, ceilings and plaster work. The chief hygienic points

which had to be continually borne in mind were:— (1) Keep the contamination from reaching clean areas, (2) Keep the workers free of activity, (3) Prevent the inhalation of material among all those concerned. The chief contaminant was radium and the dangers of its ingestion are very well known. The work was completed in 6 months; this involved removing 2 inches of concrete from some of the floors before a safety level of 0·2 mr per hour at a distance of 1ft. was registered.

S. Russ

TOLOT, F., SOUBRIER, R. & COMBY, Oedème de Quincke au ciment. **[Quincke's Oedema with Cement]** *Arch. Malad. Professionnelles.* Paris. 1961, Mar., v. 22, No. 3, 148–50.

This is a brief account of an assistant cook who developed angioneurotic oedema of pharynx, tongue, right eyelid and arm after 3 weeks of helping to build a cement stairway. This was his first contact with cement and sensitivity tests were negative to it, but positive to the constituent, potassium bichromate. For 2 months previously the patient had lost sleep and weight and had been overworking. He had hypotension and slight albuminuria. The serum showed no *histamino-pexique* power. Hospital investigations were otherwise negative, including tests for intestinal parasites. Antihistamines had controlled the condition, but the patient showed a tendency to depression and later the skin lesions recurred. The aetiology is discussed, particularly with reference to the low state of general health in an allergic subject. Though there was apparently no history of previous contact with the allergen, the hypochlorite solutions handled in his kitchen work contained potassium bichromate as a stabilizing agent.

M. Patrícia Fitzsimons

VÁMOS, L. & VINCZE, Erzsébet. Az epoxy (aethoxylin) gyanták elöállítása és alkalmazása közben kifejlödött börártalmak. **[Occupational Dermatoses produced by manufacturing and using Epoxy Resins]** *Munkavédelem.* Budapest. 1961, v. 7, Nos. 1/3, 49–52.

Epoxy resins are used for insulation of electric instruments. Some of the hardeners added to the liquid epoxy resin cause skin irritation. Positive reactions were found by GRANDJEAN [this *Bulletin*, 1957, v. 32, 592] using Araldite and hardener 951 [triethylenetramine] for patch testing. Similar results were found by the authors, mainly in the clinically serious cases. Most of the examined persons were exposed to Araldite vapour, because between the mixing of epoxy resin with hardener and its transformation into the solid state, the hardener evaporates from the mixture. The primary symptoms were erythematous itchy patches and these appeared on forearm, cheek, neck and eyelid. After recovery the epidermis remained permanently allergic to the substance concerned.

Ladislaus Magos

PALMINTERI, G. Le dermatiti da persolfati nel quadro dell'eczema professionale dei fornai. **[Persulphate Induced Dermatitis in relation to Bakers' Eczema]** *Med. d. Lavoro.* 1961, Jan., v. 52, No. 1, 53–8. [12 refs.] English summary.

It has long been recognized that flour, lactic acid, yeast, chlorine, soap and many other agents may be the cause of dermatitis in bakers. There has been a marked increase in this disorder since persulphate came into use to check the proteolytic action of certain enzymes in the gluten and thus to produce a mixture of greater uniformity. When flour thus treated is used the persulphate is partly destroyed but certain authors have shown that excessive amounts may be present even if these are not harmful to those eating the bread.

The author found dermatitis in 30% to 50% of operatives in places where persulphate was used. The fingers and forearms were most affected and the rash was an eczematous involvement of the epidermis. Tests for sensitivity might be positive after 7 or 8 hours, showing microvesicular erythema. Once sensitivity has developed it may continue indefinitely but cases are known in which bakers, no longer exposed to persulphate, though their employment had not changed, remained free of trouble. It appears that sensitivity to persulphate may develop in as short a time as 2 months and not rarely by the 8th month of exposure, whereas untreated flour or flour not containing this material takes much longer before any allergic troubles occur. But in general, though further use of persulphate may be undesirable, it remains true that an eczematous eruption of the type described seems to pave the way to sensitivity to many other materials, and flour is one of these. It seems desirable therefore that persulphate should no longer be used in bakeries.

G. C. Pether

BANDMANN, H. J. & NASEMANN, T. Bäckerekzem durch eine Lebensmittelfarbe der Azofarbstoffreihe. **[Baker's Eczema due to an Azo Dye for Colouring Food Stuffs]** *Berufsdermatosen.* Aulendorf. 1961, Apr., v. 9, No. 2, 79–84.

This report on a case of baker's eczema due to an azo-dye is presented because references in the literature to such cases are few.

The baker who had no history of allergic reactions suffered a severe eczema of both hands and forearms which began with an itching of the left hand shortly after the hand, owing to damage of the rubber glove he was wearing, had come into contact with the mixture used in the manufacture of the product known as "Brezeln".

An extensive series of skin tests were carried out and the results of these are detailed. The materials used in the tests included standard substances, the red rubber of the gloves and the dyestuffs used by bakers. Positive results in these tests were obtained with the red azo-dye used in foodstuffs, Ponceau Red 6R, certain parasubstituted dyestuffs and also with the red rubber of the gloves the baker used. The chemical composition of

these gloves remains unknown to the authors of the paper. The existence of this group allergy is discussed shortly. *M. E. Delafield*

SCHMIDT, W. Über Vorkommen und gutachtliche Beurteilung von chronischen Paronychien in Nahrungsmittelbetrieben. [**Incidence and Expert Evaluation of Chronic Paronychia encountered in the Food Industry**] *Berufsdermatosen.* Aulendorf. 1961, Apr., v. 9, No. 2, 65–71. [14 refs.]

Chronic paronychia in confectioners was described 80 years ago. The literature is referred to and there is a considerable description and discussion of the condition with mention of the fact that the disease is not restricted to confectioners but occurs also in brewers, housewives, workers with vegetables and chocolate and in many other occupations. There is also a full clinical account of a case of paronychia with involvement of the fingernails in a confectioner.

It is stated that a large proportion of cases are the result of *Candida* infections and that most of these infections have in recent years been reported from countries and occupations in which manual handling has not been superseded by mechanical methods.

In the case described *Candida albicans* was isolated from the fingernails and the sputum and *Geotrichum candidum* from the faeces. *M. E. Delafield*

ASHE, W. F.; CARTER, E. T.; HOOVER, G.; ROBERTS, L. B.; JOHANSON, E.; BROWN, F.; LARGENT, E. J., Jr. **Some Responses of Rats to Whole Body Mechanical Vibration. Part I** [ASHE, CARTER, HOOVER, ROBERTS, JOHANSON, BROWN & LARGENT]. *Arch. Environment. Health.* Chicago. 1961, Apr., v. 2, No. 4, 369–77, 4 figs. [14 refs.] **II. Metabolic Gas Exchange** [CARTER, LARGENT & ASHE]. *Ibid.*, 378–83, 4 figs.

Part I of this paper begins with a short review of the literature dealing with studies of the effects of vibration on experimental animals and on man. The animal experiments have mostly been carried out on animals which were restrained or anaesthetized or both, and it is considered that the extrapolation of results so obtained to the normal animal, free to adjust to vibration, may not be justified.

The authors used adult white rats. These were exposed to mechanical vibration on a shake-table. Vibrations in the horizontal and in a vertical plane were used. The frequencies of vibration ranged from 3 to 26 cycles a second (c.p.s.), and movement of the vibrating floor of the cage was almost purely sinusoidal. The amplitudes of vibration were 0·062, 0·125 and 0·25 inch, giving whole-body total displacements of 0·125, 0·25 and 0·50 inch respectively.

Changes in body temperature and weight and in blood counts and blood sugar were observed.

At any given combination of frequency and amplitude 3 animals were used, and these were never used at other vibration parameters. When results appeared equivocal the number of animals was increased to 9. Control animals sat in cages in the same room as the test animals but were not vibrated.

The outstanding effect of the vibration was on the body weight, and on the basis of weight-loss the stress of vibration was much more severe in the vertical plane than in the horizontal. At frequencies of 3 c.p.s., and to a less extent at 5 c.p.s., at any amplitude, the animals usually lay down and slept. At higher frequencies the vibration was stressful, and the animals were continuously busy moving about in the attempt to protect themselves. Above 15 c.p.s., as the animals became exhausted, their heads began to vibrate and their feet slid out to the sides. Only frequencies of 20 and 26 c.p.s., at an amplitude of 0·25 inch were lethal in these experiments.

No changes were found in the red cell count, haemoglobin or blood sugar. On all first runs there was a fairly consistent fall in the white cell count, but it is suspected that this may have been a non-specific response to stress. No definite evidence of acclimatization to vibration was found.

Part II describes the results of measurements of the effect of vibration on the respiratory gas exchanges. The rats were subjected to vibration at the frequencies and of the amplitudes used in the experiments described in Part I of the paper, and their respiratory exchanges were measured at regular intervals. There was no increase in the gas exchange at an amplitude of 0·062 inch whatever the frequency. At an amplitude of 0·125 inch there was an increased respiratory exchange at frequencies above 15 c.p.s., and at 0·25 inch an increase occurred at frequencies above 5 c.p.s.

Thomas Bedford

Food and Nutrition

The order in this section is:—**General; Foodstuffs; Food Poisoning.**

FOODSTUFFS

Composition and Bacteriological Control

WOOD, P. C. **The Production of Clean Shellfish.** *Roy. Soc. Health J.* 1961, May–June, v. 81, No. 3, 173–7, 3 figs. [22 refs.] Discussion 177–8.

This is a clear and comprehensive account of the various methods of shellfish purification which have now been shown to be sound and feasible trade practice in Britain. The original Dodgson installation, which is logical and reliable, has been found too costly for general adoption, but the same principles can be applied and can achieve equally safe results with a simpler technique in more economical installations. Thus, a small tank installation has been constructed inside a shed and has been operated successfully, with Chloros as a chlorinating agent, by a producer in Fowey for some years. At Brightlingsea it is now possible to save considerably on fuel as the self-purifying physiology of the oyster remains effective at a much lower temperature of the tank water than was thought to be the case by Dodgson. Dechlorination by thiosulphate can be omitted as we now know that the chlorine has been used up within 1½ hours of being added, and the shellfish then proceed to function naturally and cleanse themselves. In Teignmouth, where the estuary water is only lightly polluted, the action of the mussels themselves has been found sufficient, without any added sterilizing agent, to purify the tank water and then the shellfish.

The amount of heating of periwinkles which is necessary before the meat can be picked out of the shell is enough to sterilize them, and constitutes an automatic safeguard.

Wood also deals briefly with the sterilization of cockles and mussels by steam as it is carried out at Southend (Leigh-on-Sea) and elsewhere. *J. Cauchi*

SYLVESTER, P. K. & GREEN, J. **The Effect of Different Types of Cooking on Artificially Infected Meat.** *Med. Officer.* 1961, Apr. 21, v. 105, No. 16, 231–35, 5 figs.

Joints of meat (topside beef and legs of mutton) were heavily contaminated with cultures of coagulase-positive staphylococci, *Salmonella typhi-murium* and heat-resistant sporing *Clostridium welchii*; sometimes the cultures were inserted deeply on blotting paper into the meat. Some of the joints were roasted in the orthodox manner and some overnight in a slow gas oven (Regulo ¼) for about 17-18 hours, the inside of the meat reaching 150°F. in 6½–9 hours and remaining at this temperature. The temperatures of each joint were recorded in the centre and on the surface during the experiments by a multipoint temperature recorder.

The salmonellae and staphylococci were killed during both methods of roasting. The *Cl. welchii* survived in the overnight roasted meats to a greater extent than in the joints roasted in the orthodox manner.

Inconclusive results were obtained on the survival of *Cl. welchii* during overnight stewing at ¼ Regulo of steak artificially inoculated with a culture, but *Cl. welchii* was easily recovered after one experiment. 16 samples of gravy made from the juice of uninoculated meat stewed overnight were also examined with negative results.

It is recommended that cooking overnight should not be done. *Betty C. Hobbs*

See also p. 887, GEORGE & PAYNE, **Tuberculosis from T. T. Milk, with Note on the Frequency of *Brucella abortus* in Consumer Milk.**

FOOD POISONING

HARVEY, R. W. S. & PHILLIPS, W. P. **An Environmental Survey of Bakehouses and Abattoirs for Salmonellae.** *J. Hygiene.* 1961, Mar., v. 59, No. 1, 93–103. [29 refs.]

31 of 111 (27·9%) gulley swabs taken from bakehouse floor drains were positive for salmonellae, *Salm. typhi-murium* (8), Salm. Aberdeen (12), and Salm. Thompson (9); *Salm. paratyphi B* was found twice.

15 of 93 swabs from staff sewage were positive, *Salm. typhi-murium* on 8 occasions, *Salm. paratyphi B* twice, Salm. Aberdeen once, and Salm. Thompson not at all; staff infection probably came from contaminated goods. 3 of 42 samples of out-flow water from staff wash-hand basins were positive for *Salm. typhi-murium* and Salm. Aberdeen. Salm. Thompson and Salm. Virchow were isolated from swabs wiped over the surface of bakehouse machinery even after routine cleansing (one cake mixer). Chinese frozen egg used daily was visible on the hands and forearms of bakery staff and on floors and tables.

Two outbreaks of food poisoning spread by baker's confectionery had been reported in the area during the last 5 years [see also below].

Of 247 swabs from gullies in abattoirs, 111 were positive for salmonellae (40·5%); 21 different serotypes

were isolated of which *Salm. typhi-murium* was the commonest, and Salm. Dublin next in frequency. 17 of the serotypes have been found in animal feeding-stuffs.

Of 30 phage-typed *Salm. typhi-murium* from human infections (mostly sporadic) in the area, 23 belonged to phage types found in the abattoirs and on local farms, and the time of isolation often corresponded. There was also a tendency for human cases of salmonellosis due to other serotypes to occur in the local population in the same quarter of the year as samples from abattoirs were found positive for the same serotypes.

MOORE's gauze swabs [this *Bulletin*, 1949, v. 24, 187] were used throughout, incubated at 43°C. in single strength selenite broth containing 1 in 10^6 brilliant green and subcultured at 24, 48, 76 and 96 hours on to brilliant green MacConkey agar and Loureiro's modification of Wilson and Blair bismuth sulphite agar [*ibid*, 1942, v. 17, 649] incubated at 37°C. and examined at 24 and 48 hours. *Betty C. Hobbs*

HARVEY, R. W. S., PRICE, T. H., DAVIS, A. R. & MORLEY-DAVIES, R. B. **An Outbreak of *Salmonella* Food Poisoning attributed to Bakers' Confectionery.** *J. Hygiene.* 1961, Mar., v. 59, No. 1, 105–8.

Of 270 children attending a Christmas party more than 100 were taken ill 8-78 hours afterwards with vomiting and diarrhoea, headache and colic for approximately 26 hours. 25 children were admitted to hospital and there were 209 persons with positive faecal swabs. *Salm. typhi-murium*, phage type 2c and Salm. Thompson phage type 4, were isolated from remnants of trifles eaten at the party. *Salm. typhi-murium* was isolated from 4 bakery staff (2 with symptoms), a girl who had handled the luncheon meat, 2 drain swabs and 117 patients. Salm. Thompson was isolated from 23 patients, and both serotypes from 69.

The phage types of both salmonellae suggested an egg product as the source of infection, and this had been used in the cake included in the trifles.

Betty C. Hobbs

SHAPIRO, S. E., ZHDANOV, I. S., BARYSHNIKOVA, A. I., KIREEVA, P. I., CHAPOVSKAIA, L. G., KRUPNIKOVA, A. M. & PODKOSOVA, N. I. **Analysis of an Outbreak of Paratyphoid B caused by Infected Hen's Egg Products.** *J. Microbiol., Epidemiol. & Immunobiol.* London. 1960, v. 31, No. 6, 1021–7. [Translated from Russian.]

An outbreak of *Salm. paratyphi B* in Khabarovsk occurred towards the end of May 1958; commencing with 5 cases it rose to a peak during the first 10 days of June with 47 cases, and gradually decreased until the middle of September, when there were no further cases. Patients were scattered all over the town, and the disease affected mainly children of school and preschool age of 4–15 years. Clinical symptoms are described; they were severe in 10%, moderate in 67% and mild in 23% of cases. There was no correlation between illness and social or occupational distribution of the adults. There were no fatal cases. The morbidity was usually limited to one case per family, apartment, or house.

Transmission of infection by water, milk and dairy products and bakery products was excluded. Investigation of ice-cream manufacturers showed that an imported egg mixture had been used as one of the constituents. The method of pasteurizing the half-finished product had not been checked nor had the ice-cream been subjected to bacteriological examination. The ice-cream was grossly contaminated and the egg mixture was found to contain 3 strains of *Salmonella paratyphi B*, 7 strains of *Salm. typhi-murium*, Salm. Aberdeen, "*Salm. bovis*" and *Salm. bovis morbificans*.

Biochemical, cultural and serological properties of 10 strains of salmonellae isolated from the egg mixture, from 8 patients, and one carrier identified the strains and established a connexion between the cases and the consumption of ice-cream. The use of egg mixture in ice-cream was discontinued and the remains of the contaminated product were destroyed.

The evidence indicated that in 75% of cases the infection was due to the consumption of ice-cream, and in 4% there was transmission by contact. The examination of 52 imported hen's eggs gave negative results.

It was concluded that the use of imported hen egg mixtures should be permitted only under conditions determined by the sanitary legislation concerning duck and goose eggs, that is, their open sale should not be permitted and they should be used in bakeries and for pastry production only. *Betty C. Hobbs*

HAYASHI, K., KUGITA, Y., NAITO, T. & HARA, K. **[Co-operative Production of Poisoning Substances by Halophile Bacteria and *viridans* Streptococci isolated from Food Poisoning Cases in a certain Large Dockyard in Nagasaki City]** *Endem. Dis. Bull. Nagasaki Univ.* 1960, Dec. 23, v. 2, No. 4, 248–54, 1 fig. [In Japanese.]

The English summary appended to the paper is as follows:—

"Some strains of halophile bacteria, related to *Pseudomonas ichthyodermis*, and *viridans* streptococci were isolated from the remains of lunch (whale bacon) and vomitus in an incident with 680 cases of food poisoning in a certain large dockyard in Nagasaki city. Diarrhea was seen in kittens which were given food extract soiled by these halophile bacteria, and vomiting fits in them occurred after giving one soiled by *viridans* streptococci. More severe diarrhea with vomiting fits in kittens was observed after giving the food extract soiled by these two isolated bacteria together or one again soiled previously by *viridans* streptococci and then by halophile bacteria. By the development of paper chromotography of these soiled extracts, it was worthy of attention that there always were spots reactive to ninhydrin which ran up to 0·45, 0·65 and 0·74 of Rf, and these substances seemed to have relation to foregoing toxic symptoms of kittens."

HAYASHI, K., KUGITA, Y., TAWARA, M. & YAMAGATA, H. **[Mass Food Poisoning caused by *Clostridium welchii* Hobbs Type 2]** *Endemic Dis. Bull. Nagasaki Univ.* 1961, Mar. 23, v. 3, No. 1, 1–9. [19 refs.] [In Japanese.]

[This abstract is from the author's summary in English].

The authors report on an outbreak of food poisoning (309 cases) in Nagasaki, Japan. The source was fried fish paste (*agekamaboko*). The onset was acute, with vomiting and diarrhea and, in serious cases, intestinal bleeding. There was one death. The usual food poisoning organisms could not be isolated, but anaerobic culture of vomitus, food left over, stools and intestinal washings from a dead person gave strains of a heat-resistant, Gram-positive, non-motile, capsulated anaerobic bacillus. These were identified as *Clostridium welchii* Hobbs type 2. None of the freshly isolated strains reacted to the standard immune sera against types 1 to 11 in the agglutination test, but did so after being heated at 100°C. for 1 hour and after repeated subculture in liver broth. Agglutinin titres of 1 in 20 to 1 in 40 were found against the isolated strains in convalescent sera. *Charles Wilcocks*

Mycoses and Mycology

The order of diseases and fungi in this section is:—**General; Dermatophytes; Blastomyces; Histoplasma, Sporotrichum, Phialophora; Candida, Cryptococcus; Actinomyces, Nocardia; Aspergillus; Others.**

Papers on Blastomycosis (South American type), Coccidioidomycosis, Mycetoma and Rhinosporidiosis are abstracted in the TROPICAL DISEASES BULLETIN.

MCDONOUGH, E. S., AJELLO, L., AUSHERMAN, R. J., BALOWS, A., MCCLELLAN, J. T. & BRINKMAN, Sherry. **Human Pathogenic Fungi recovered from Soil in an Area Endemic for North American Blastomycosis.** *Amer. J. Hyg.* 1961, Jan., v. 73, No. 1, 75–83, 1 pl. [27 refs.]

[An abstract of this paper appeared in the *Tropical Diseases Bulletin*, 1961, v. 58, 1073.]

BRESLAU, A. M., HENSLEY, T. J. & ERICKSON, J. O. **Electron Microscopy of Cultured Spherules of *Coccidioides immitis*.** *J. Biophysic. & Biochem. Cytol.* Baltimore. 1961, Mar., v. 9, No. 3, 627–37, 10 figs. [23 refs.]

PICKETT, J. P., BISHOP, C. M., CHICK, E. W. & BAKER, R. D. **A Simple Fluorescent Stain for Fungi. Selective Staining of Fungi by means of a Fluorescent Method for Mucin.** *Amer. J. Clin. Path.* 1960, Sept., v. 34, No. 3, 197–202, 9 figs. (8 coloured on pl.)

A rapid and simple staining method for fungi is described in detail. The fluorescent dye used was acridine orange. The preparations, after staining with Weigert's iron haematoxylin, were counterstained with acridine orange. A blue light fluorescent filter was used when viewing the preparation.

A number of pathogenic fungi treated by this method appeared as follows: *Actinomyces* sp. (red to yellow), *Coccidioides immitis* (yellow-green), *Cryptococcus neoformans* (red), *Histoplasma capsulatum* (red to yellow), *Aspergillus* sp. (green), *Candida albicans* (yellow-green), *Blastomyces dermatiditis* (yellow-green), *Nocardia asteroides* (not stained), *Rhinosporidium seeberi* (red), *Blastomyces brasiliensis* (yellow), *Monosporium apiospermum* (yellow-green), *Rhizopus* sp. (not stained).

This staining process, which can be carried out in 10 to 15 minutes, should be a useful addition to staining methods already in use for routine examinations.

C. J. La Touche

VÖRÖS-FELKAI, G. & NOVÁK, E. K. **Incidence of Yeasts in Human Material.** *Acta Microbiologica.* Budapest. 1961, v. 8, No. 1, 89–94. [29 refs.]

STORCK, H. Klinik und Immunbiologie der Mykosen. **[Clinical and Immunological Features of Mycoses]** *Schweiz. med. Woch.* 1961, Apr. 22, v. 91, No. 16, 474–9, 7 figs.

This and the 2 succeeding papers were read at a post-graduate course in the Faculty of Medicine, Zurich. This is a general account of the superficial mycoses (actinomycosis is also mentioned) dealing with the source of infection, clinical features (with 14 photographic illustrations) and the course of the disease. There are also 2 ingenious although rather crude diagrams, of which the second represents the degree and rate of development of allergy and immunity in

different classes of infection, the underlying principle being that when only avascular structures such as hair are involved these reactions do not occur, but their intensity increases with the depth of involvement of vascular tissue. Information is also given about the changing incidence of different dermatomycoses: whereas ringworm and tinea cruris are much less common, others have become more frequent, including *Epidermophyton rubrum* infection of the nails, athlete's foot (perhaps because of greater indulgence in sport), and infections by *Candida albicans*, thought to be due to the greater frequency of diabetes and to the use of broad-spectrum antibiotics. *L. P. Garrod*

Burckhardt, W. Die Behandlung der Dermatomykosen. [**The Treatment of Dermatomycoses**] *Schweiz. med. Woch.* 1961, Apr. 22, v. 91, No. 16, 479–82. [10 refs.]

Mycoses are classified as to whether they respond or not to treatment with griseofulvin. If they do, the duration of treatment depends on the thickness of the epidermal structure affected. In an infection of the inguinal region, 4–5 weeks suffices: if the skin of the hands or feet is involved it may sometimes be necessary to continue for 8 weeks or more, and for infections of the nails, those of the fingers need 3–4 and those of the feet 5–8 months. Infections insusceptible to griseofulvin are erythrasma, pityriasis versicolor, candidiases, and actinomycosis. Several formulae are given, containing salicylic acid, undecylenic acid, iodine or zinc salts, suitable for the local treatment of the first 3 of these conditions. *L. P. Garrod*

Fischer, E. Zur Technik des Pilznachweises bei mykotischen Erkrankungen. [**Methods of Demonstrating Fungi in Mycotic Diseases**] *Schweiz. med. Woch.* 1961, Apr. 22, v. 91, No. 16, 482–3.

The author points out that many mycological diagnoses can be verified by simple means. He gives instructions for mounting skin scrappings or nail parings in clearing fluids (xylol or caustic potash solution) or staining fluids such as lactophenol blue, and refers to the use of Gram's stain for exudates. Histology, cultivation and serological methods, which call for the help of a fully equipped laboratory, are dealt with more briefly. *L. P. Garrod*

Padilha Gonçalves, A. Micoses superficiais. (Atividades do setor de micologia do Departamento de Dermatologia da Policlínica Geral do Rio de Janeiro em 1959 e 1960.) [**Superficial Mycoses. Activities of the Mycological Section of the Dermatology Department of the General Polyclinic in Rio de Janeiro in 1959 and 1960**] *Brasil-Médico.* 1960, Nov.–Dec., v. 74, Nos. 45/52, 437–50. [24 refs.] English summary.

Vanbreuseghem, R., Dekeyser, P. & Lauwers, R. Culture sur terre non stérile de divers dermatophytes. [**Culture of Dermatophytes in Non-Sterile Soil**] *Ann. Soc. Belge de Méd. Trop.* 1960, Apr. 30, v. 40, No. 2, 415–21.

The authors describe experiments in which they demonstrated the ability of certain dermatophytes to grow in both sterile and non-sterile soil inoculated with hair parasitized by these dermatophytes or artificially inoculated with them.

Guineapig hair which had been inoculated 15 days previously with *Trichophyton mentagrophytes* was deposited on sterile soil, unsterile soil and unsterile soil plus fowl manure. This dermatophyte was able to grow on the first two types of soil but not on that which contained the fowl manure, nor, as was shown later, on soil containing human excrement. Another experiment of a somewhat similar nature showed that it could grow on soil containing rabbit droppings, and a third experiment in which horse hair parasitized by this fungus was deposited on sterile and on unsterile soil also resulted in the growth of the dermatophyte on these media.

A similar result was obtained with calf hair parasitized by *T. verrucosum* and guineapig hair inoculated with *Microsporum canis*.

The authors conclude from these results that certain dermatophytes at least are able to change from a parasitic life on hair to a saprophytic one in the soil. *C. J. La Touche*

Vanbreuseghem, R., with the technical collaboration of R. Lauwers. Un cas d'herpès circiné d'origine tellurique causé par *Microsporum gypseum*. [**Tinea Circinata due to *M. gypseum* from Soil**] *Ann. Soc. Belge de Méd. Trop.* 1960, Apr. 30, v. 40, No. 2, 409–13. [10 refs.]

This article records a case of tinea circinata due to *Microsporum gypseum* in a boy aged 5½ years.

On examination he presented with a lesion on his right knee. 1 month previously this knee had been scratched when he fell on the ground near a house in Leopoldville in the Congo. Direct examination of scrapings from the lesion revealed mycelium in the lanugo hairs, some of which were also surrounded by irregularly formed sheaths of spores. Cultures yielded *Microsporum gypseum*.

Subsequent investigations of the soil near the house in Leopoldville where the patient had fallen resulted in the isolation of *M. gypseum* from 2 samples.

The author concludes from these results that infection in this case was due to a strain of *M. gypseum* which was living as a saprophyte in the soil. *C. J. La Touche*

Grayson, L. D. & Shair, H. M. **Griseofulvin: Systemic Therapy for Superficial Fungal Infections.** *Clin. Pharmacol. & Therap.* St. Louis. 1960, Sept.–Oct., v. 1, No. 5, 624–30. [12 refs.]

166 patients with fungal infections of the scalp, nails or skin were treated orally with griseofulvin. "The

initial dose was usually 1,000 mg. daily in four divided doses." This was gradually reduced to 125–250 mgm. daily, and continued at this level for 2–6 weeks after clinical and laboratory evidence of cure.

The most important feature of the results obtained in this series was the recurrence of infection in a number of patients who had been discharged as clinically clear. Thus, there was recurrence of infection in 13% of tinea cruris patients, in 3% of tinea corporis and 20% of tinea manuum. In addition, "approximately one-fourth of the cases caused by *T. rubrum* [*Trichophyton rubrum*] and *T. mentagrophytes* returned clinically". *C. J. La Touche*

See also p. 876, SCHMIDT [**Incidence and Expert Evaluation of Chronic Paronychia encountered in the Food Industry**].

BALŞ, M., SERBĂNESCU, Florica, CĂRUNTU, F., TAINDEL, C. & JIPA, G. Frecvența alergiei specifice la histoplasmina la bolnavii internați în clinica a II-a de boli contagioase, Bucuresti. [**The Incidence of Specific Histoplasmin Allergy in Patients hospitalized in the Second Clinic of Contagious Diseases, Bucharest**] *Microbiol., Parazitol., Epidemiol.* Bucharest. 1961, Mar.–Apr., v. 6, No. 2, 147–53.

The English summary appended to the paper is as follows:—

"After a brief review of some general data on histoplasmosis and its world-wide distribution, on the basis of three cases with a histopathologically confirmed diagnosis, the authors discuss the researches carried out on cutaneous histoplasmin allergy in 321 patients hospitalized for various acute or subacute febrile affections. A net positive skin reaction was found after 24 and 48 hours in 4 cases (1·2%), more transient reactions in 3·7%, and doubtful reactions in 6% of the cases. In none of the cases did the epidemiologic, clinical and roentgenologic findings indicate possible histoplasmosis."

STRAUB, M. & SCHWARZ, J. **General Pathology of Human and Canine Histoplasmosis.** *Amer. Rev. Respiratory Dis.* 1960, Oct., v. 82, No. 4, 528–41, 12 figs. [23 refs.]

After briefly reviewing the pathogenesis of histoplasmosis as hitherto described in the literature, the authors record their findings in 55 autopsies of patients in the Jewish hospital in Cincinnati, as well as their autopsy investigations of 100 dogs.

In the dogs they found calcified foci in the lungs in 20%, while in 11% "calcified tracheobronchial lymph nodes were also present." No abnormality could be demonstrated in the spleens of any of these animals by X-ray examination.

The lesions consisted of "calcified necrotic tissue floating in amorphous chalky material in which many cholesterol clefts could be recognized". After decalcification, *Histoplasma capsulatum* organisms could be demonstrated in them, sometimes in large numbers.

Pulmonary or splenic X-ray investigations of human subjects revealed lesions in 84·6% from endemic areas and in 87·5% from non-endemic areas. Infection in adult life involved only the lymph node or nodes draining the infected area, whereas in childhood the lymph nodes were extensively involved. The lesions in adults were dry and caseous and showed little or no calcification.

In some cases lesions in adults were of the "coin lesion" type, a histoplasmoma, which is thought to be the result of primary infection during adult life. This form of histoplasmosis is found "mainly in adults less than fifty years of age" and usually outside the endemic areas, whereas cavitary histoplasmosis occurs mainly in subjects aged from 50 to 60 years and is found mainly within the endemic areas. Endogenous reinfection is thought to be the cause of cavitary histoplasmosis but the possibility of exogenous reinfection cannot be ruled out. *C. J. La Touche*

ANN. SOC. BELGE DE MÉD. TROP. 1960, Apr. 30, v. 40, No. 2, 293–307, 2 text figs. & 4 figs. on 2 pls. [35 refs.] Contribution à l'étude de l'histoplasmose au Katanga. I. Étude clinique. Histoplasmose pulmonaire à forme miliaire. [**Histoplasmosis in Katanga. I. Pulmonary (Miliary) Form**] [BOVY, P.]. II. Considérations écologiques sur l'histoplasmose [**II. Ecology of Histoplasmosis**] [ANCIAUX DE FAVAUX, R. P. F.]. III. Étude mycologique. Mise en évidence d'histoplasmes dans une grotte [**III. Mycology; Presence of the Organism in a Cave**] [PATTYN, S. R. & DELVILLE, J. P.].

This article records the main clinical and radiological features of pulmonary histoplasmosis in 4 patients, a male student aged 20 years, his 2 sisters aged 19 years and 17 years, and a fellow speleologist, all of whom lived in the Congo and had recently visited some caves on 26th July, 1959. Ecological studies in the various caves are also described. These included exposure of mice to the atmosphere of the caves, as well as injection of mice with suspensions of soil from the caves. These mice were then subsequently investigated for the presence of *Histoplasma capsulatum* in their organs.

In all 4 patients X-ray examination revealed disseminated miliary lesions in the lung fields. Marked symptoms in 2 of the patients were cough, dyspnoea and asthenia, while in the other 2 (sisters of the male student) symptoms were minimal. Histoplasmin skin tests were positive in all 4 patients as well as in the majority of their fellow speleologists.

Treatment was symptomatic pending the arrival of a supply of amphotericin B; and at the end of a week all 4 patients had responded well to it. Moreover, all symptoms had disappeared in 3 of the patients and were much diminished in the fourth. Eventually, when the supply of amphotericin B arrived, it was considered unnecessary to use it and, in the following December, recovery was still being maintained in all the patients.

H. capsulatum was isolated from 1 of the mice

exposed in one of the caves which the speleologists had visited, but not from the mice which had been injected with soil suspensions. The strain which was thus isolated had low pathogenicity for experimentally infected mice. *C. J. La Touche*

LUNN, H. F. **A Case of Histoplasmosis of Bone in East Africa.** *J. Trop. Med. & Hyg.* 1960, Aug., v. 63, No. 8, 175–80, 9 figs. [21 refs.]

Lesions in bone due to infection by *Histoplasma capsulatum* have been rarely reported in the literature [see this *Bulletin,* 1960, v. 35, 555].

The patient concerned was a Muganda schoolgirl aged 13 years. She gave, on admission, a history of intermittent pain and swelling in her left leg, extending over 6 months, and stated that, 3 weeks prior to admission, "the skin over the anterior aspect of her left tibia had broken down and a sinus had formed"; also, her right index finger had become painful and swollen.

On admission she was "toxic, febrile and in pain. The left leg was swollen and tender below the knee". X-ray examination of the lesions revealed destruction of bone, but no involvement of the periosteum, except for a linear periosteal accretion in the affected area of the tibia.

Operation revealed, in the medulla of the tibia, a yellowish-grey material of cheesy consistency which histologically suggested "acute purulent osteomyelitis with numerous giant cells surrounding suppurative lesions". Subsequently an operation on the right index finger revealed, at the centre, necrotic debris, which on histological examination revealed giant cell systems and caseation necrosis. Staining for acid-fast organisms revealed large numbers of highly refractile bodies identified as *Histoplasma duboisii.* These bodies had also been recognized in biopsy material collected at an earlier date from the lesion in the tibia. Positive cultures could not be obtained from either lesion.

The post-operative course, as regards both lesions was uneventful, with steady progressive resolution. In the meantime, other lesions developed, 1 in the distal part of the right radius and the other in the left fibula. These lesions also resolved subsequently to surgical intervention.

During the post-operative period of convalescence the patient was given a course of diamino-diphenylsulphone in the dosage of 100 mgm. daily for 2 months, and then 200 mgm. daily for 10 months.

C. J. La Touche

ZIPRKOWSKI, L., ALTMAN, G. & KRAKOWSKI, A. **[Sporotrichosis]** *Harefuah.* Jerusalem. 1961, Apr. 16, v. 60, No. 8. [In Hebrew 252–3, 2 figs. English summary 253.]

The English summary appended to the paper is as follows:—

"A short review of the recent literature on sporotrichosis is presented. A case of sporotrichosis of the cutaneous fixed type with misleading clinical and histological picture is described. The diagnosis could only be made by means of a culture. In retrospect, the case history fitted the diagnosis, and the rapid recovery following treatment with potassium iodide confirmed the diagnosis. The possible causes of diagnostic error are noted and the importance of an awareness of the possibility of sporotrichosis is stressed."

STAIB, F. & BRAUN, H. *Candida tropicalis* bei pathologischen Lungenbefunden. **[*Candida tropicalis* in Lung Disease]** *Deut. med. Woch.* 1961, May 12, v. 86, No. 19, 940–44, 970–71. [20 refs.]

The English summary appended to the paper is as follows:—

"During five years Candida tropicalis was isolated from the sputum of 220 patients admitted to the University Department of Medicine in Würzburg. In 40 of them this fungus was found consistently and in abundant numbers. The associated lung disease was not uniform: pneumonia, bronchopneumonia, bronchitis, emphysema, bronchiectasis, tuberculosis and bronchial carcinoma were found. In 19 of 33 patients there was considerable growth of C. tropicalis before chemotherapy; in 15 administration of antibiotics and chemotherapeutic agents had preceded the isolation of C. tropicalis. In most instances abundant fungal growth was associated with abnormal bacterial findings, which were probably principally responsible for the inflammatory changes. Massive chemotherapy was employed in 22 patients with abundant growth of C. tropicalis and resulted in healing clinically. But in the majority of cases C. tropicalis was isolated from the sputum in abnormal amounts, despite evidence of healing of the pulmonary disease. A mycosis due to C. tropicalis, following chemotherapy, was observed in two patients."

ROBERTS, F. B. **Recovery from Monilial Septicemia.** *Canadian Med. Ass. J.* 1960, Oct. 15, v. 83, No. 16, 857–60. [21 refs.]

A case of monilial septicaemia is described, in which the patient, a girl aged almost 16 years, recovered spontaneously. The various types of monilial infection are, in addition, reviewed.

The case report shows that, on admission, the patient gave a recent history of pain in the right calf which spread to involve the entire limb. "She was short, mentally retarded and cyanosed, and had marked clubbing of the fingers and toes".

On the assumption that the patient was suffering from thrombophlebitis, anticoagulant therapy was instituted, but was discontinued after a week when it was not found possible to obtain a stable prothrombin time. Also, since a haemolytic streptococcus was grown in blood cultures, the diagnosis was changed to bacterial endocarditis. Penicillin was accordingly administered intramuscularly in the dosage of 2·4 million units daily. As a result of this the patient's temperature fell, and, at the end of the second week of this treatment the pain in her leg ceased.

At the end of the 3rd week of treatment cellulitis of the right lateral calf developed, and penicillin dosage was increased to 30 million units by intravenous route daily. As a result of this increased dosage the cellulitis gradually resolved.

At the end of 6 weeks of penicillin therapy cellulitis developed around the intravenous catheter. Blood culture then yielded *Candida albicans*, and this was also recovered from various other sites including the mouth and urinary bladder.

Nystatin (1,200,000 units daily) was administered orally, and, during the 2 weeks following the initiation of this treatment the patient gradually recovered.

C. J. La Touche

KAY, J. H., BERNSTEIN, S., FEINSTEIN, D. & BIDDLE, Marjorie. **Surgical Cure of *Candida albicans* Endocarditis with Open-Heart Surgery.** *New England J. of Med.* 1961, May 4, v. 264, No. 18, 907–10, 4 figs. [23 refs.]

"A brief review of the clinically important, but meagerly documented, entity of fungous endocarditis is presented. The contributing factors to candida sepsis are described, with particular emphasis on the role of prolonged antibiotic intravenous therapy in cases of underlying bacterial endocarditis.

"A well documented case in which actual proof of fungous growth of *Candida albicans* within the heart was made during life is described. Cure of a defect of the ventricular septum, as well as removal of the infected portion of the tricuspid valve, was accomplished with open-heart surgery. This is the first known report of a cure of subacute bacterial endocarditis with surgical excision of the vegetations from a portion of a cardiac valve. The failure of amphotericin B to eradicate systemic candidiasis is emphasized".

BAUM, G. L. & ARTIS, Dorothy. **Growth Inhibition of *Cryptococcus neoformans* by Cell Free Human Serum.** *Amer. J. Med. Sci.* 1961, May, v. 241, No. 5, 613–16, 1 fig. [21 refs.]

These experiments were conducted to see if the known bactericidal effect of cell-free human serum applied to *Cryptococcus neoformans*. Sera from 10 persons, 3 normal and 7 diseased, were used and the experiments were done in parallel with both unheated and heated (56°C. for half an hour) serum.

Serial dilutions of *C. neoformans* ranging from 5 to 5,000,000 cells per ml. were prepared in a mixture of Sabouraud's dextrose broth 2·25 ml. and human serum 2·25 ml. and incubated at 37°C. for 10 days. Thereafter, pour plates of Sabourand dextrose agar and 0·5 ml. of *C. neoformans* culture from each of the above tubes were made, incubated at 20°C. and examined after 4, 7 and 15 days. In addition controls consisting of the same dilutions of *C. neoformans* in pure dextrose broth were similarly treated. The pour plates also incorporated penicillin 1,000 units per ml. and streptomycin 2,000 units per ml. [which seems an unnecessarily large amount of antibiotic].

The controls gave heavy growth of *C. neoformans* at all dilutions. With *C. neoformans* 5,000,000 cells per ml. in serum + broth, growth was moderate to heavy; under the same conditions, *C. neoformans* at 500 cells per ml. failed to grow in all but 2 of the sera and no growth occurred with 5 cells per ml. in any serum. There was no significant difference between the heated and unheated serum in this respect.

The conclusion is that there is a heat-stable factor in cell-free human serum which is inimical to *C. neoformans*. [The results would be more convincing if the controls had been arranged to contain as much protein as the serum-broth tubes]. *Ian G. Murray*

KREJCÍ, O., VYSOKÁ, B., HANZAL, F., ŘEHÁNEK, L. & MANYCH, J. Generalizovaná kryptokokóza (torulóza). **[Generalized Cryptococcosis (Torulosis)]** *Časopis Lékařů Českých*. Prague. 1961, Apr. 21, v. 100, No. 16, 484–92, 10 figs. [33 refs.] English summary.

The authors describe a case of a generalized cryptococcosis in a worker aged 59 years employed in a sugar factory.

In August 1957 he started to complain of general malaise, tiredness and "heaviness" in his chest; his temperature rose gradually to 38·9°C. An X-ray examination of the chest showed that he was suffering from pneumonia. He was treated with penicillin, but there was no response; although no tubercle bacilli were found in his sputum, an active tuberculous process was suspected and he was treated accordingly. The temperature occasionally rose above 37°C. His lung condition remained the same.

In the middle of October he started to complain of headaches and one week later meningeal signs appeared. Lumbar puncture showed a large number of leucocytes and erythrocytes. The spinal fluid was turbid and under pressure.

A microbiological investigation, which included an experimental inoculation of the spinal fluid into white mice, proved that the infective agent was *cryptococcus neoformans*.

The patient died on 8th November.

A post-mortem examination revealed: Brain: in frontal sections minute cavities, the size of a pin head, containing translucent fluid; Lungs: in both apices blackish-grey, tough fibrotic deposits; both apices were adherent, the right base contained a tumour the size of a walnut. There were no notable changes in the other organs. Histological examination of the brain showed the typical cryptococcus; indentical findings were present in the right base of the right lower lobe of the lungs. Both apices showed old tuberculous lesions.

The treatment so far is unsatisfactory: Amphotericin B may be the drug of choice. *Paul Frankl*

DORMER, B. A. & FINDLAY, M. **Generalized Cryptococcosis with Osseous Involvement.** *South African Med. J.* 1960, July 16, v. 34, No. 29, 611–13, 4 figs.

The patient concerned was a Bantu male aged 14 years who gave a history of having been under treatment for typhoid fever.

Shortly after admission he developed a swelling of the left upper eyelid which appeared to be a sebaceous or meibomian cyst. Soon after this, he complained of a pain in the left ankle. This became swollen, and X-ray examination revealed an erosion in the os calcis: accordingly a plaster cast was fitted. The swelling in the left orbit increased in size, and eventually discharged a muco-pus spontaneously. Other lesions then developed, including osteitis of the 9th rib on the left side of the chest, a lesion in the xiphisternum, lesions in the cervical spine, and later, an erosion in the left anterior superior iliac spine.

Laboratory investigations revealed a yeast-like fungus on culture which was thought at first to be of *Candida* type but later was identified as *Cryptococcus neoformans*.

Intravenous Amphotericin B was accordingly administered commencing on the 3rd June, 1959. "A polythene catheter was inserted into the inferior vena cava *via* the right saphenous vein and a continuous drip containing amphotericin B was started with a concentration of 0·25 mg. per kg. for the first day, increased to 0·5 mg. the next day, and then up to 0·75 mg. per kg." The concentration was kept at this level for the first 6 days. However, owing to pyrexia supervening subsequently the concentration was dropped back to 0·25 mgm. per kgm., at which level there was practically no reaction. The drip was then continued at this level of concentration for another 10 days.

The results of this treatment were very gratifying; X-rays showing that progressive resolution of the bony lesions had set in, and that the lung fields were clear.

The patient was discharged shortly afterwards, on the 26th October, 1959. *C. J. La Touche*

Buitrago-García, E. & Gómez-Arango, S. Comprobación de un caso de criptococosis. [**A Case of Cryptococcosis in Caldas, Columbia**] *Caldas Méd.* Manizales. 1960, Dec., v. 1, No. 2, 5–16, 6 figs. [53 refs.] English summary (4 lines).

This is a description of a case of generalized cryptococcosis, the first proved example in Caldas, Columbia. *Cryptococcus neoformans* of a strain virulent to mice was isolated from the patient's lesions.

Amphotericin B was administered intravenously with good results as far as the short follow-up has gone.

Ian G. Murray

Smith, D. E. & Benecke, J. **Pulmonary Nocardiosis. Report of a Fatal Case.** *Med. J. Australia.* 1960, Aug. 13, v. 2, No. 7, 254–8, 8 figs. (4 on pl.) [21 refs.]

The patient concerned in this case was a female aged 56 years.

On admission on June 16th, 1959 she gave a 5-day history of "malaise, heaviness in the head, shivers and vague chest pain, which was not suggestive of pleurisy." She was thought to be suffering from an influenzal type of infection and was, accordingly, given phenoxymethyl penicillin orally in the dosage of 250 mgm. every 6 hours. She became seriously ill on June 25th "with toxaemia, cyanosis, a temperature of 103°F. and clinical signs of consolidation of the lower lobe of the left lung".

Despite further treatment, commencing with procaine penicillin and sulphadiazine, the patient's condition steadily deteriorated and she died on July 2nd, 1959.

At autopsy a number of "grey, firm, bronchopneumonic lesions" were found which were undergoing confluence. These measured from 0·2 to 2·0 cm. in diameter.

Smears from these pulmonary lesions revealed "numerous Gram-positive, filamentous branching organisms". They were also acid-fast in preparations stained with Ziehl-Neelsen and decolourized for 5 minutes with sulphuric acid diluted to a concentration of 1%. Cultures from these lesions yielded *Nocardia asteroides*.

Histological examination showed an inflammatory and necrotic process in the terminal bronchioles and alveoli. There was no tubercle formation, nor were giant cells observed. There was no involvement of any other organs.

The biological and pathological features of *Nocardia* are discussed at length.

[For an account of another case and review of the literature, see also this *Bulletin*, 1957, v. 32, 577.]

C. J. La Touche

Gale, G. R. & Welch, Ann M. **Studies of Opportunistic Fungi. I. Inhibition of *Rhizopus oryzae* by Human Serum.** *Amer. J. Med. Sci.* 1961, May, v. 241, No. 5, 604–12, 7 figs. [13 refs.]

This work was prompted by the previous observations of others of the fungistatic properties of human serum and the organism selected for study was *Rhizopus oryzae* from a fatal human case of cerebral mucormycosis. Serum was collected from routine blood donors, umbilical cords of newly born babies and 6 diabetics (4 well controlled, 1 in acidosis and 1 recently dead of widespread carcinoma).

Culture was carried out in 50 ml. Erlenmeyer flasks to each of which was added 4 ml. Sabouraud broth (at 5 times normal concentration), 1 ml. of a 0·005% spore suspension of *R. oryzae*, 1 drop of 5% chloramphenicol, serum and diluent (buffered saline, distilled water or plain 0·9% saline) to a total of 20 ml. The volumes of serum and diluent were adjusted to give final serum concentrations ranging from 0 to 30 or 35% in 5% steps. The flasks were incubated at room temperature on a shaker, generally for 18–20 hours but in one series also for 42 and 66 hours. After incubation the mycelium was filtered off, washed, blotted, dried at 75° C. for 18 hours and weighed to the nearest 0·1 mgm. Replicate weighings showed the deviation from the mean to be less than 5% if the spore suspension was thoroughly mixed before inoculation.

Normal serum at 5–10% stimulated growth of *R. oryzae*; higher concentrations progressively inhibited growth at 20 hours and inhibition was virtually complete at 20–30%. Umbilical cord serum behaved similarly but did not inhibit as strongly. Serum heated to

56° C. for 2 hours, serum freed from properdin by adsorption on inulin and zymosan and sera from the 4 controlled diabetics all inhibited *R. oryzae* at 20 hours in the same way as normal adult serum.

Serum treated with activated charcoal or dialysed against distilled water lost its inhibitory power. Adult serum dialysed against 0·9% saline acquired enhanced stimulating power at under 10% but lost most of its inhibitory power at higher concentrations.

Sera from the diabetic in acidosis and from the one dead of carcinoma had scarcely any inhibitory power. As the acidosis was brought under control the patient's serum acquired a slight inhibitory power.

A partially purified globulin fraction from normal adult serum failed to inhibit *R. oryzae*.

Prolonged incubation allowed *R. oryzae* to overcome the inhibitory effect of human serum. At 42 and 66 hours growth was much stimulated at serum concentrations up to 30%. At 35% serum and 42 hours incubation, inhibition became total, but at 66 hours, though growth was declining, it was still far in excess of that in plain Sabouraud broth.

This is an interesting paper. The number of diabetics in the series is too small to justify theorizing but the results point to the need for further study of such persons and their known predisposition to infection by fungi belonging to the order Mucorales.

Ian G. Murray

Communicable Diseases

The order in this section is:—**Tuberculosis; Venereal Diseases; General Infective Diseases; Other Communicable Diseases.**

For the bacteriology of these diseases see the section on Bacteriology below. For diseases conventionally regarded as tropical, readers are referred to the TROPICAL DISEASES BULLETIN

TUBERCULOSIS

SHENNAN, D. H. **The Evolution of Tuberculosis in Southern Rhodesia. Part I. History: The Introduction and Spread of Infection before 1890.** *Central African J. of Med.* 1960, Aug., v. 6, No. 8, 352–5, fig. 1. **Part II. Pathogenesis: the Relation of Infection to Disease.** *Ibid.*, Sept., No. 9, 395–8. **Part III. Examination: A Comprehensive Tuberculin Survey of the African School Children of Manicaland.** *Ibid.*, Oct., No. 10, 432–46, figs. 2–7. [22 refs.]

In the first part of this series of papers the author touches briefly on the history of tuberculosis in the southern part of Africa, and particularly on the fact that an earlier tuberculin survey in Bulawayo and Mashonaland showed lower rates of infection than a recent survey in Manicaland, a rural area.

From the records in Southern Rhodesia it seems that the case-mortality rate showed a sharp decline in 1951–54 as a result of the introduction of the new drugs, but since then there has been no indication of a further fall from this cause.

The author discusses the fact that the resistance of Africans to tuberculosis is on the whole low, and refers to the effect of urban and industrial life in Africans brought up in very different circumstances, and to their parasitic infections.

In the third part the author gives the results of a survey of 44,106 African schoolchildren aged 5–18 who were tested with 5 TU of OT by the intradermal route. The general tuberculin positive rate was 40·6%, rising from 23% at age 5 (21·3% at age 6) to 69·9% at age 18, boys having slightly higher rates than girls. The author calculates a comparative sensitivity index (CSI) for the various areas surveyed, which is the total number of positives discovered in the group, divided by the number which would have been found if the group had had standard rates; the standard rates were those given by the first 6,000 children tested. On this basis he observed that the highest infection rates occurred in hot, low-lying areas where individual resistance is presumed to be sapped by the oppressive heat and the prevalence of schistosomiasis and malaria. Hilly country apparently discourages the spread of infection. Reactor rates were lower in towns than in similarly situated African areas, probably because the housing conditions are better in the towns, but though the tuberculin rates were lower in the town the actual tuberculous disease rates were higher, probably because resistance is lowered by unaccustomed labour and an alien environment; many of the men engaged in industry are single and live in conditions tending to lower resistance. On farms the tuberculin rates were rather lower than in the African areas.

Infection and disease rates, therefore, were low in rural areas at higher altitudes, and on farms; infection and disease rates were high in low-lying rural areas and rural industrial areas; infection rates were low, but disease rates were high, in towns. Certain remote areas seem so far to have avoided heavy infection.

Charles Wilcocks

CARIBBEAN MED. J. 1960, v. 22, Nos. 1/4, 122 pp., 2 text figs. & 7 figs. on 2 pls. [13 refs.] **Tuberculosis in the West Indies.**

This symposium is concerned with tuberculosis in the British West Indies Federation and British Guiana. The Federation consists of 10 island territories with a total population of some 3,115,000 chiefly of African, East Indian and European descent. British Guiana, on the mainland, has a population of 557,960 including about 22,000 aboriginal Indians. The mainstay of the territories is agriculture but mineral development, including petroleum, is proceeding.

H. P. S. GILLETTE (Federal Medical Adviser) states that there was little tuberculosis in the islands until 1836 after which time it quickly became a prominent cause of death in children and young adults. Control measures began to be undertaken by various bodies in individual territories and in 1952–56 WHO carried out a programme of BCG vaccination.

J. H. THOMAS (Federal Chest Physician) contributed general comments on respiratory tuberculosis throughout the region. Improvement in communications had lessened the difference between urban and rural areas so that the disease is becoming more evenly distributed than previously. Inter-island travel is increasing with the result that susceptible adults from remote districts visit areas where tuberculosis is endemic and run the risk of infection.

Chemotherapy is highly effective but in many cases it fails because the disease is too far advanced for permanent cure. Laboratory facilities for testing drug sensitivity are being provided increasingly but as yet there are not enough surgical units. Case-finding techniques need to be improved, X-ray units are insufficient and contact examination must be extended to cover a wider range than at present.

The resistance of individuals to the disease appears to increase progressively from the low level seen in the Amerindians of British Guiana through the higher levels seen in Africans and East Indians to the highest level exhibited by the Chinese and European patients. At each stage a typical pattern of the disease is seen but these patterns are becoming less distinct.

Children in the West Indies do not often suffer from tuberculous meningitis, miliary or acutely progressive primary disease, and tuberculin conversion is usually uneventful. The incidence of skeletal and renal tuberculosis is not unduly high in adults, and the disease is usually limited to the lungs. It often progresses rapidly unless treated, and Thomas postulates a peculiar failure of lung resistance, an increased invasiveness of the tubercle bacillus or massive reinfection to explain the clinical findings.

Tuberculosis was found to carry an unwarranted stigma in all the territories visited; this is diminishing but is still serious enough to hinder case finding and the re-employment of ex-patients.

Although there is more tuberculosis in some islands than in others it is common in all. There is a lack of balance between the various tuberculosis services, and the best means of achieving inter-island co-operation would be to give the Federal Government power to initiate, co-ordinate and control the tuberculosis programme throughout the whole region.

[As the above extracts present a fairly complete picture of the tuberculosis situation in the West Indies let it suffice to record that the remaining contributors to the symposium deal with tuberculosis in animals, clinical aspects of the disease in man and the results of treatment, epidemiological findings in individual territories and methods of prevention and control already in operation or recommended. The whole symposium is of great interest and value.] *H. G. Calwell*

SZENT-GYÖRGYI, N. **Risk of Tuberculous Infection and of Radiation among University Students.** *Amer. Rev. Respiratory Dis.* 1961, Mar., v. 83, No. 3, 432–5. [Refs. in footnotes.]

The hazard of excessive exposure to radiation is at present a frequent subject of comment. X-ray examination is an essential procedure in tuberculosis control and care should be taken to use it as safely as possible and only where and when necessary.

The author used his previous experience of the epidemiology of tuberculosis in students in the United States [this *Bulletin*, 1958, v. 33, 109] as the basis of a control programme in which the frequency of X-ray examination was determined by the incidence of the disease in various groups.

The student population in the University of Chicago was divided into 2 groups; the first ("general risk") consisted of white students born in North America, and the second ("special risk") consisted of non-white and foreign-born students, tuberculosis workers and medical students engaged in clinical work. At the entrance examination every student was X-rayed and tested with intermediate strength PPD unless recorded as a previous reactor or as having been vaccinated with BCG or having, or having had, tuberculosis. The "general risk" group was to have skin tests and X-ray examination every 3 years only and the "special risk" group annually. This modified programme was introduced in 1958.

During the period 1958–60 4,192 students were examined. It was found that 11% of those tested were reactors; the rates were 5·9% and 32·5% in the general risk and special risk groups respectively. These rates showed a marked improvement over those found in 1955 [*loc. cit.*].

The rate of tuberculin conversion was 0·9% for the general risk group and 6·4% for the special risk group. No satisfactory explanation was found for the great difference of the conversion rate between the 2 groups. The number and percentage of converters was found to have fallen steadily and significantly from 1955. This was evidence of the success of the control measures used.

The proportion of converters and reactors did not change significantly between the 2 groups during the period 1958–60. 4 students were found to have active pulmonary tuberculosis, 1 in the general risk group and 3 in the special risk group.

These findings are taken to support the author's view that the proper grouping of a population may decrease

the frequency of X-ray examinations and the accompanying radiation hazard without impairing the control of tuberculosis in a community. *H. G. Calwell*

GEORGE, J. T. A. & PAYNE, D. J. H. **Tuberculosis from T.T. Milk, with a Note on the Frequency of *Brucella abortus* in Consumer Milk.** *Monthly Bull. Ministry of Health & Pub. Health Lab. Service (directed by Med. Res. Council).* 1961, May, v. 20, 99–102.

"Milk-borne tuberculosis, including tuberculous adenitis, was commonplace 30 years ago. Since the extensive adoption of pasteurization and the institution of the Attested Herds Scheme, this type of infection has become comparatively rare in England and Wales. Unfortunately, two accepted measures, taken to ensure the freedom of milk from tuberculosis, are at present being performed less effectively than hitherto. On the one hand there is a general tendency throughout the country to take fewer samples for biological testing and, on the other, there is a planned extension of time between routine tuberculin tests of cattle."

The authors fear outbreaks of milk-borne tuberculosis if progressive relaxation is to be the current policy, and their comment quoted above is supported by an account of cervical adenitis in two 9-year-old schoolchildren; investigation which followed showed that 31 of 128 cattle supplying school milk reacted to the tuberculin test. It was a TT herd. 8 of 44 children tested with tuberculin were subsequently found to react. One of the 8 had an enlarged left submandibular gland.

Two further breakdowns in attested herds are also recorded; a slaughtered bullock from an attested herd had a tuberculous lymph gland and it was then discovered that there were 43 reactors in the herd of 118; dates are given, and the extreme rapidity with which the breakdown proceeded is noted. Another breakdown had been discovered initially in the slaughter house; 35 reactors were subsequently found and about 20 gallons of milk from this herd was retailed daily in a village. The purchasers of the milk were traced and 76 children, nearly half of those examined, were positive to the tuberculin test; 3 had enlarged cervical glands.

The relevant veterinary officer and medical officer in the latter area have agreed to inform each other of cases of bovine tuberculosis of the udder or of the milk on the one hand, and of any suspected spread of tuberculous infection from human sources to cattle on the other hand; this latter may thereby necessitate identification of the type of tubercle bacillus concerned.

A brief record is given of the results of testing milk for the presence of *Brucella abortus*. Samples of consumer milk in the North Riding of Yorkshire show 28 of 361 positive by biological tests; 41 others were positive by the milk ring test. None of 379 samples, which were not tested biologically, reacted to the milk ring test. Attention is drawn to the fact that much of the milk-borne undulant fever is due to drinking milk from TT herds and that cases of undulant fever are occurring in the area from which these samples were collected. *R. Lovell*

RIDDELL, J. **A Serial Tuberculin Survey of Children in the County of Midlothian.** *Tubercle.* 1961, Mar., v. 42, No. 1, 18–24.

The object of this enquiry was to try and ascertain if there is any particular age at which children in the county of Midlothian, Scotland, undergo tuberculin conversion. The tuberculin jelly test was used on as many children as possible at the age of 3½ years and repeated on the non-reactors at 4½, 5½ and 6½ years. In the remotest areas it was only possible to include children when they first came to school at the age of 5½ years. The survey began on 1st January 1955, and ended in March 1959.

Positive or doubtful reactors to the patch test had confirmatory tests with the Heaf gun, and PPD. Reactors and their adult household contacts were X-rayed; child contacts were tested and if positive X-rayed also.

There were 1,996 children who would reach the age of 3½ years in 1955, and of these 1,530 were tested and 50 found to react (3·3% of those tested). At age 6½ years 1,319 were tested; 160 (12·1%) had positive jelly tests and 63 (4·8%) positive Heaf tests.

There were differences between the children in the town of Musselburgh (population 18,124) and elsewhere in the county. In the town the Heaf reactor rates were 15·8% at 3½ and 21·6% at 6½; elsewhere the rates were 1·2% and 2% respectively. In the town the jelly and Heaf tests agreed fairly well but in the remainder of the county 1·5% were positive to the jelly test and 1·2% to the Heaf test at 3½ whereas at 6½ years the rates were 10·1% and 2·0% respectively. An explanation of this marked discrepancy was sought but not found.

The considerable excess of reactors in Musselburgh was not proportionate to the known incidence of tuberculosis in the town, which was not greatly in excess of that in the rest of the county. Contact with a known case and overcrowding played some part.

There was apparently no major increase in reactor rates on entry to school.

All 63 child reactors were X-rayed and kept under observation; none developed tuberculosis. All household and other close contacts of the reactor children were fully investigated and only 1 was discovered to have tuberculosis. The investigation was therefore of little value in case finding. *H. G. Calwell*

CHAPMAN, J. S. **The Adequacy of Present Criteria of Noninfectiousness as measured by Tuberculin Conversion in the Offspring of Adults with Active Tuberculosis of the Lung.** *Amer. Rev. Respiratory Dis.* 1961, Mar., v. 83, No. 3, 436–8.

The main object of this study was to determine if patients with pulmonary tuberculosis who have been discharged from hospital in a satisfactory state, *i.e.* with negative sputum cultures, are truly non-infectious. Subordinate to the main study was the question whether the discovery of tuberculin conversion in a contact indicates relapse of the disease in an adult.

There were 51 families with a total of 231 children. An adult in each family had been treated for pulmonary

tuberculosis and had remained in continuous contact with the children following discharge. [It is stated that most of the patients were treated in hospital; their sexes are not given, nor their relationship to the children. It is therefore not possible to judge the closeness of contact. That of a mother with an infant would for example be closer and more dangerous than that of a father.]

19 of the 231 children were X-rayed and not tuberculin tested. The results of serial Mantoux tests with 5 TU of PPD or OT were available for 212. 3 months after the start of the parent's treatment there were 146 children of whom 55 (37%) were reactors. Tested after the parent's return to the household, or after birth following return, were 67 children, 1 of whom converted. With all exclusions for various reasons stated there were 125 children who were followed for an average period of 3·2 years of contact following the parent's return. The only case of conversion was that mentioned in which a boy aged 6 years was infected by his mother. Her disease had been inactive for 10 years and reactivation was discovered before the boy's re-examination.

The families in this group were living in an unfavourable economic environment in which infection if present would be likely to show itself by illness in the children. Chapman therefore concludes that present cultural methods for tubercle bacilli seem to be adequate for the establishment of non-infectiousness. *H. G. Calwell*

Shaw, R. K. & Hallett, W. Y. **Biopsy of the Parietal Pleura.** *Amer. J. Med. Sci.* 1961, May, v. 241, No. 5, 593–601, 3 figs. [33 refs.]

This paper records the results of parietal pleura biopsy by the Vim-Silverman needle technique in 42 patients. A definite diagnosis was made in 11 patients, of which one was proved to be incorrect. In 15 of the 31 patients with inconclusive needle biopsies the aetiology of the pleural effusion was determined by other methods. Pleural effusion cultures were positive in 6 patients, bacilli being grown in 3. Pleural fluid cytology revealed malignant cells in one patient. Surgical biopsy of the pleura demonstrated tuberculosis in 2 patients, carcinoma in 2, and histoplasmosis in 1 patient. Of the 31 patients who had chronic pleuritis or inadequate tissue obtained by needle biopsy 8 had tuberculous pleuritis, in 12 tuberculosis was presumed, malignancy in 3, non-tuberculous empyema in 3, histoplasmosis in 1, and 4 were uncertain. The findings of a non-specific chronic pleuritis did not rule out serious underlying disease.

A summary of previous needle biopsy of the parietal pleura reports is recorded, and also a summary of previously reported surgical biopsies of pleura. No complications apart from one pneumothorax, were reported.

F. H. Young

Mydlil, F., Procházka, J. & Mezenský, L. **Frequency of Non-Tuberculous and Tuberculous Infection of the Bronchial Stump of Lungs resected for Tuberculosis.** *Tubercle.* 1961, Mar., v. 42, No. 1, 14–17.

This paper investigates the presence of infection in bronchial stumps of 150 resected lungs, or parts o lungs. 2 patients had a non-tuberculous condition, on an aspergilloma, and another a chondro-hamartoma, th remainder had pulmonary tuberculosis. Both these had a non-tuberculous infection of the bronchial stump In only 7, out of the other 148, was any non-tuberculou infection found. The presence of tubercle bacilli in th sputum before operation had no bearing on the fre quency of the non-tuberculous infections.

In 148 tuberculous patients, 39% of the bronchia swabs were positive for tubercle bacilli, 51 patients ha positive sputum culture immediately before operation 33 had become negative, and no tubercle bacilli coul be demonstrated in 66 of the patients throughout thei sanatorium stay. Of the patients positive before opera tion bronchial swabs gave positive cultures in 45 (89%) Growth was obtained on media containing 1 μgm. pe ml. of isoniazid in 36 (80%) of the patients. Only patients had cultures resistant to 10 μgm. per ml. o streptomycin, and 14 to 10 μgm. per ml. PAS. Nega tive cultures were obtained from some patients wh were sputum positive before operation. Cultures wer taken also from resection specimen cavities; in only 1 o the 43 cavity lesions was a secondary infection found The small proportion of non-tuberculous infection demonstrated in this series is, in the opinion of th authors, due to the fact that bronchoscopies had no been done during the 2 months before the operation

F. H. Young

Kalinowski, S. Z., Lloyd, T. W. & Moyes, E. N **Complications in the Chemotherapy of Tuberculosis. A Review with Analysis of the Experience of 3,148 Patients.** *Amer. Rev. Respiratory Dis.* 1961, Mar., v. 83, No. 3, 359–71. [72 refs.]

This paper deals with 3,148 adult patients sufferin from pulmonary tuberculosis who received antitubercu lous chemotherapy between 1953 and 1959. The reviev of the complications is confined to those caused b streptomycin, PAS and isoniazid. 2,660 patients were a risk to streptomycin, 2,248 to isoniazid, and 2,940 t PAS.

The authors divide the reactions into allergic an toxic. Among the allergic complications, rashes wit or without fever, or fever alone, accounted for a hig proportion—301 out of 310 complications. Of thes 99 were reactions to streptomycin, 155 to PAS, and non to isoniazid itself, with 53 to streptomycin and PA in combination, and 3 to streptomycin, PAS and isonia zid combined. Reactions are discussed in an interestin way. Toxic complications occurred 74 times, wit vestibular disturbance and deafness accounting for 5 of the complications, all of course due to streptomycin Hepatitis which occurred in 6 patients with PAS, wa thought to be an allergic reaction. The toxic reaction are dealt with in detail.

A table is also given of rare reactions which a described in the literature but not seen in the serie quoted.

[A survey of this magnitude does not appear to hav

been undertaken before and is an excellent summary which should be read *in extenso* by all those who are interested in the subject.] *F. H. Young*

SCHWARTZ, W. S. & MOYER, R. E. **One-Half Gram of Streptomycin Daily with Isoniazid and PAS used as a Re-Treatment Regimen in Pulmonary Tuberculosis.** *Amer. Rev. Respiratory Dis.* 1961, Feb., v. 83, No. 2, Pt. 1, 268–71.

212 tuberculous patients were treated with a regime consisting of 0·5 gm. of streptomycin, 12 gm. of PAS, 300 mgm. of isoniazid daily; all patients were being re-treated. They were divided into 2 groups, those who had less than 3 months' treatment, and those who were treated for more than 3 months. In those who were treated for less than 3 months, 4 had vertigo or other neurological effects from streptomycin, and 7 had allergy to streptomycin. Among those who had treatment for more than 3 months, 2 had vertigo and ataxia from the streptomycin and 6 had allergy to streptomycin. As many patients were over 40 years old this dosage of streptomycin seems relatively free from serious neurological toxic effects.

Therapeutically, the regime was effective when the strain of tubercle bacilli was susceptible to all 3 drugs, but it was only moderately successful where there was resistance to one drug and definitely unsatisfactory where there was resistance to more.

The authors conclude that this regime is unsuitable for patients until their bacillary susceptibility has been determined. Tables are given showing the disappearance of cavities and tubercle bacilli in various groups. *F. H. Young*

MOUNT, F. W., ANASTASIADES, A. A. & SCHNACK, G. A. **Control Study of Biologically Active Isoniazid in Serum of Children with Primary Tuberculosis.** *Amer. Rev. Respiratory Dis.* 1961, Feb., v. 83, No. 2, Pt. 1, 173–83, 6 figs. [13 refs.]

In a recent clinical trial on the prophylactic effect of daily isoniazid it was found that a daily dose of 4 to 6 mgm. per kgm. could protect most children, but a certain number developed clinical tuberculosis [this *Bulletin*, 1958, v. 33, 455]. As there did not seem any other good reason it was thought possible that some of these children were rapid inactivators of isoniazid. Accordingly, 770 children, some who had been given isoniazid and some who were controls, were given a test dose of 8 mgm. of isoniazid per kgm. of body weight. A specimen of blood was drawn after 2 hours, and a further specimen after 6 hours. 97% of the children had serum concentrations of at least 1·6 μgm. of active isoniazid per ml. 2 hours after a single dose of 8 mgm. per kgm. Approximately 35% had at least 6·4 μgm. of isoniazid, 43% had 3·2 to 6·3 μgm. and 19% 1·6 to 3·1 μgm. Little difference was found between the treated children and those who were the controls.

After 6 hours the children had a mean of 1·3 μgm. for the treated children and 1·4 μgm. for the untreated. No difference was noted between the children whose tuberculin sensitivity had changed. Low isoniazid concentrations were not found to be more frequent among those children who had unfavourable pulmonary changes. There was some evidence that extrapulmonary complications were a little more common in the children whose serum concentrations were low, but the figures do not give sufficient basis for a conclusion to be drawn. *F. H. Young*

NAITÔ, M., WATANABE, R., TSUKUMA, S. & IBA, K. **Antituberculous Activity of Isoniazid in combination with Sulfisoxazole (Gantrisin) I. The Effect of Isoniazid-Sulfisoxazole *in vitro*.** *Acta Tuberculosea Japonica.* 1960, Sept., v. 10, No. 1, 47–56. [10 refs.]

Isoniazid in combination with sulphafurazole (Sulfisoxazole) has been used for some years in Japan in the treatment of pulmonary tuberculosis. This paper deals with the *in vitro* effect.

It was found that the addition of sulphafurazole to PAS or streptomycin had no additive tuberculostatic effect, whereas in combination with isoniazid the effect was from one-half to one-sixth better. This was confined to conditions when the concentration of inoculum was higher than 0·04 mgm. per ml. of the medium. The combined effect was not apparent when the concentration of inoculum was less than 0·004 mgm. per ml. of medium.

The combined effect of the 2 drugs was more marked in an acid than in a neutral or an alkaline medium. The advantage was maintained when tubercle bacilli resistant to streptomycin and PAS were used. It was also found that the emergence of resistance to isoniazid was delayed by adding 3 to 10 times as much sulphafurazole, especially in a neutral medium. *F. H. Young*

JORDAHL, C., DES PREZ, R., DEUSCHLE, K., MUSCHENHEIM, C. & MCDERMOTT, W. **Ineffectiveness of Nicotinamide and Isoniazid in the Treatment of Pulmonary Tuberculosis.** *Amer. Rev. Respiratory Dis.* 1961, June, v. 83, No. 6, 899–900.

"A group of 33 previously untreated patients with moderately and far advanced pulmonary tuberculosis were treated with nicotinamide and isoniazid for a minimal period of three months. After three months of therapy only 11 patients had shown substantial roentgenographic improvement and 4 had already shown clinical deterioration. At the six-month period, reversal of infectiousness had occurred in only 9 of the 33 patients who received nicotinamide with isoniazid, compared with a 72 per cent. incidence of reversal of infectiousness in a previous clinical trial with isoniazid alone. The total clinical results with isoniazid-nicotinamide were so poor that the study was terminated in the interest of the patients, and appropriate antituberculous drugs were added to isoniazid as indicated for each individual patient. It was concluded that, in the dosages used in this study, isoniazid and nicotinamide were contraindicated as an antituberculous chemotherapy."

HANSEN, J. E. **Hypersensitivity to Isoniazid with Neutropenia and Thrombocytopenia.** *Amer. Rev. Respiratory Dis.* 1961, May, v. 83, No. 5, 744–7, 3 figs. [15 refs.]

"Hypersensitivity reactions which occur in the course of antituberculous drug therapy are most commonly due to PAS or streptomycin. They may, however, as in this case, be due to isoniazid. The patient in the present report developed thrombocytopenia and neutropenia as part of the hypersensitivity reaction."

SHORT, Eileen I. **The Estimation of Isonicotinyl Acid Hydrazide and some of its Metabolites in Urine.** *Tubercle.* 1961, June, v. 42, No. 2, 218–26, 2 figs.

BATTAGLIA, B., KAUFMAN, I., LYONS, H. A. & MARSH, W. **Toxicity of Cycloserine combined with Isoniazid in the Treatment of Tuberculosis in Children.** *Amer. Rev. Respiratory Dis.* 1961, May, v. 83, No. 5, 751–2.

"Cycloserine (20 mg. per kg.) and isoniazid (5 to 10 mg. per kg.) were administered together to infants and children with primary tuberculous infections. Concentrations of cycloserine in the blood were determined and found to be within the accepted therapeutic range. Pyridoxine and anticonvulsant drugs were not administered to these patients. There were no toxic effects from these drugs during the two-year period of this study."

CRAIG, J. W., WILLIAMS, H. & ALSTON, J. M. **Cycloserine Treatment of Out-Patients with Chronic Drug Resistant Pulmonary Tuberculosis.** *Tubercle.* 1961, Mar., v. 42, No. 1, 7–13. [16 refs.]

This paper reports the results of cycloserine treatment on 24 patients with chronic drug-resistant pulmonary tuberculosis. 16 were treated with 250 mgm. cycloserine, and 150 mgm. isoniazid every 12 hours. 8 patients selected at random were treated with the same dose of isoniazid with purified talc every 12 hours. Both groups also took 50 mgm. pyridoxine with each dose.

Of the 16 in the cycloserine group 3 had to be removed from the trial, as had 2 in the control group, owing to intolerance of the drugs. The patients were treated for 1 month in hospital and for the 11 months following, as out-patients. 4 patients in the cycloserine-isoniazid group, compared with 1 of the control group, showed radiographic improvement. 7 patients showed an improvement in clinical condition in the cycloserine group compared with 1 in the control group.

Although some patients attained a temporary sputum conversion no permanent conversions were obtained in either the control or the cycloserine group.

F. H. Young

ALLAN, G. W., LEES, A. W. & ROBERTS, G. B. S. **Trial of Ethionamide.** *Brit. J. Dis. Chest.* 196 Apr., v. 55, No. 2, 91–5.

This paper reports on 78 patients with chronic pu monary tuberculosis who were treated with ethion amide [this *Bulletin*, 1959, v. 34, 620], 1 gm. per da Therapy had to be stopped in 32 because of toxic rea tions, in 15 within 14 days, in 9 between 14 days an 3 months, and in 8 after 3 months. The early toxi effects were nausea, vomiting and anorexia. The late toxic effects were mental disturbance, swelling of th face, and skin sensitization. In all but 5 of the 5 patients who completed 3 months' therapy, ethionamid was accompanied by a drug to which the organism were sensitive. PAS, 15 gm. daily was given in 3 cases, pyrazinamide 1·75 gm. daily in 6, isoniazid 40 mgm. daily in 4, streptomycin 1 gm. daily in 3, an cycloserine 1·5 gm. daily in 1 case. Sputum conversio was obtained in 33% to 50% of these patients, a average of 41%. In 5 ethionamide alone was use because there was no available drug to accompany it in none of these was conversion obtained.

In the ethionamide-PAS patients whose sputur converted at 3 months, 7 had initial sensitivity tests of whom 3 were completely sensitive to ethionamid and others showed varying degrees of resistance. I the ethionamide-PAS patients who did not convert a 3 months, 6 out of 17 were completely sensitive, and 1 showed varying degrees of resistance. Among patient who did not convert, and in whom resistance t ethionamide developed, resistance to the accompanyin drug appeared in about half. Of those who complete 3 months' therapy, rather more than half showed som radiological improvement. Of the 5 treated wit ethionamide alone, 2 improved.

The authors conclude that ethionamide is a usefu drug, but that its value is severely limited by the rela tively frequent toxic reactions. The paper is interesting but like so many which have been published lately, it value is limited by the relatively small number o patients reported. *F. H. Young*

STEPHANOPOULOS, C. **Pulmonary Tuberculosis follow ing Treatment with Corticosteroids.** *Brit. J. Dis Chest.* 1961, Apr., v. 55, No. 2, 100–104, 7 figs. or 2 pls. [15 refs.]

This paper reports on 5 patients in whom pulmonary tuberculosis developed during treatment with cortico steroid. In 3 X-ray of the chest was normal before th start of treatment, in 1 calcified glands only were demonstrated and in 1 hilar nodes were enlarged an sarcoidosis was diagnosed. Corticosteroids were pre scribed in 2 patients for articular conditions, in 1 fo lymphogranuloma, 1 for sarcoidosis and 1 for spondyl arthrosis. In 4 of the patients pulmonary tuberculosis developed, and in a fifth, a man of 68 years of age dense bilateral miliary tuberculosis appeared. H failed to respond to any treatment and generalized miliary tuberculosis was discovered at autopsy. A short review of the literature is given,

The number of patients in whom the development of pulmonary tuberculosis has been reported during the course of corticosteroid therapy is relatively small considering the extensive use made of the drug at present, but it might be advisable for X-rays of the chest to be taken every 3 months. *F. H. Young*

LEGGAT, P. O. **The Clinical Pattern of Resistance in Pulmonary Tuberculosis.** *Brit. J. Dis. Chest.* 1961, Apr., v. 55, No. 2, 96–9.

This paper reviews the fate of 49 patients suffering from pulmonary tuberculosis who were resistant to one or more of the standard drugs. 10 of these died of the disease. 20 of the 36 living patients remained sputum-positive owing to extensive disease, multiple resistance, advanced years, and failure to cooperate. 3 others have died of non-tuberculous disease. Multiple resistance was associated with failure of sputum conversion. There were 12 (60%) such patients in the "live positive" group, and only 8 (50%) in the "live negative" group.

The author considers that development of resistance was due to bad therapy in 11 cases, but in the majority the most likely cause of failure lay in the patient's lack of persistence in taking the drugs regularly. The average age was high, and many had advanced disease; surgery was therefore feasible in only a minority.

F. H. Young

THOMAS, H. E. **A Tuberculosis Drug-Resistance Register.** *Tubercle.* 1961, Mar., v. 42, No. 1, 1–6, 1 fig. [11 refs.]

At the end of 1956 a register of patients from whom bacilli resistant to antituberculous drugs have been obtained was kept for the City of Birmingham. This paper reports on 287 patients from whom drug-resistant bacilli were isolated for the first time during the years 1956–59. Of these, 88 were resistant to isoniazid only, 16 to PAS only, and 58 to streptomycin only. This gave a total of 162 patients resistant to 1 drug, 74 to 2 drugs, and 51 to 3 drugs. Of these 287 patients 35 had drug-resistant organisms on diagnosis. 18 of these were resistant to streptomycin only, 8 to PAS only, and 5 to isoniazid only. All patients were assessed as at the last examination between the 31st December in the year in question and were placed in categories according to their condition. Assessment was made at the end of 1–2 years, 2–3 years, and 3–4 years. In those resistant to 1 drug only, the prognosis was worse in the isoniazid-resistant group than in the streptomycin-resistant group, except in the 3–4-year assessment where the position was reversed. Whereas 5% of a random sample of patients with sensitive bacilli had died at the end of the 3–4-year review, isoniazid-, PAS-, and streptomycin-resistant patients had rates of 28%, 20%, and 30% respectively. With resistance to 2 drugs the rate was 48%, and for 3 drugs 56%. It was thought that the relatively high rate of resistance to streptomycin compared with isoniazid was due to the longer period in which streptomycin has been in general use.

A convincing case is made out for the keeping of a tuberculosis drug resistance register. *F. H. Young*

COETZEE, A. M. *et al.* **The Treatment of Pleural Effusion in Bantu Mine Labourers. A Further Therapeutic Trial.** *South African Med. J.* 1961, Apr. 22, v. 35, No. 16, 321–3.

This investigation follows on one previously reported in which standard antituberculous therapy was compared with standard antituberculous therapy combined (1) with prednisolone (2) with penicillin and (3) with ascorbic acid. The results indicated that antituberculous therapy combined with prednisolone was markedly superior to the 3 other methods of treatment in pleural effusions. In this paper methyl-prednisolone (Medrol) was used instead of prednisolone. By drawing lots 2 comparative groups of patients were obtained:— Treatment T, 1 gm. streptomycin sulphate intramuscularly daily for 8 weeks and 200 mgm. of isoniazid 3 times daily for 8 weeks; Treatment TS, a similar regime was given but with the addition of 8 mgm. of methyl-prednisolone 3 times daily for 2 days followed by 4 mgm. 3 times daily for the remainder of the 8 weeks.

Of the 39 patients treated by method T, 6 (15·4%) were cured at the end of 4 weeks, and with treatment TS, 16 (40%) of 40 patients were cured; at the end of 8 weeks 14 (35·9%), and 27 (67·5%) respectively were cured.

The investigation confirms the previous report that the use of steroids accelerates the absorption of the pleural effusions to a statistically significant degree. No evidence was obtained that methyl-prednisolone was superior to prednisolone.

[See also this *Bulletin*, 1960, v. 35, 456.]

F. H. Young

BRITISH TUBERCULOSIS ASS. **A Report from the Association's Research Committee** [THOMPSON, B., Chairman]. **Relapse in Pulmonary Tuberculosis: an Analysis of the Fate of Patients notified in 1947, 1951 and 1954.** *Tubercle.* 1961, June, v. 42, No. 2, 178–86, 1 fig.

"Random samples of patients notified as having pulmonary tuberculosis at 15 centres in England and Scotland in the years 1947, 1951 and 1954 were followed-up and the relapse rates determined. Of the 2,269 in the samples, 1,862 (82·1%) were traced. The disease in 362 (19·4%) of these patients never became quiescent; the proportion was 45·0% among those notified in 1947 and 10·8% among those notified in 1954.

"Of the 171 notified in 1947 who were classed as quiescent, the relapse rate, calculated by the life-table method, was 3·7% in the first year and 7·9% in the 3rd year; thereafter the yearly relapse rate remained

between 1·8% and 4·7% up to 9 years. Of the 875 notified in 1954, the rates for the first four years were 2·6%, 3·1%, 2·2% and 0·7%.

"The relapse rates in men aged 45 or more were higher than in women of the same age group. The likelihood of relapse appeared to be much more influenced by the type and duration of chemotherapy than by the original extent and nature of the pulmonary disease.

"The importance of prolonged observation of patients with pulmonary tuberculosis after apparent arrest of the disease is emphasized."

DALOUS, A., SALLANOVA, J. & BLANCHARD, M. Étude du pronostic lointain de la méningite tuberculeuse de l'enfant. [**The Remote Prognosis of Tuberculous Meningitis in Children**] *J. Méd. de Bordeaux.* 1961, Apr., v. 138, No. 4, 562–4.

During the period 1949–57 the authors treated 152 children aged 6–14 years suffering from tuberculous meningitis. 79 died (52%), and of the 73 survivors 50 attended for review during the 3 months to March 1960. The survival rate was only 24% in 1949 but in 1957 it was 100%.

Hemiplegia of mild degree was present in 5 children. It had been recorded during the acute illness in a number of children in whom there was now no sign of it. There was facial paralysis in 1 child. All 6 children were able to live normal lives.

1 child had convulsive attacks from which he had not suffered before his illness. They began about 3 years after the onset of the meningitis and were not recorded during the acute illness. Conversely a number of children who had had convulsions during the acute stage were now free from them. Electroencephalographic examination showed normal or almost normal tracings in 88%.

Choroidal scarring was seen in 3 children (6%) although tubercles had been seen in over 20% at the start. Atrophy of the optic nerve was present in 6, 4 of whom had impairment of visual acuity. There was no case of blindness, and 2 children with oculomotor paralysis still had binocular vision.

It was possible to carry out hearing tests in 45 children. 12 (24%) had no cochlear lesion, 2 had deafness for sounds of high frequency only, 9 had impairment of hearing of normal conversation and 16 were totally or grossly deaf. Vestibular disturbance was not severe; only 1 child suffered from vertigo.

Intelligence tests showed that the intelligence quotient was below 80 in 6 children (16%), 80–90 in 10 (26%) and above 90 in 22 (58%).

It was concluded that 7 children (14%) were completely cured, 13 (26%) were clinically normal, 12 (24%) had impairment of minor degree, and 18 (36%) were severely incapacitated, of whom 16 were totally deaf. 14 of these 16 had received intrathecal streptomycin. This sequel should be seen rarely in future since the abandonment of that form of treatment in the majority of cases. The prognosis should therefore be favourable especially considering the therapeutic progress that has been made by the introduction of isoniazid and the corticosteroids with a resultant diminution in the incidence of drug resistance and blockage of the circulation of the cerebrospinal fluid.

H. G. Calwell

GAISFORD, W. & GRIFFITHS, Margaret I. **A Freeze-Dried Vaccine from Isoniazid-Resistant B.C.G.: A Clinical Investigation.** *Brit. Med. J.* 1961, May 27, 1500–501.

The use of a vaccine prepared from an isoniazid-resistant strain of BCG would permit the vaccination of persons actually exposed to tuberculous infection if isoniazid were administered simultaneously until the occurrence of post-vaccinal tuberculin conversion [see CANETTI, this *Bulletin*, 1957, v. 32, 18]. The chemoprophylaxis would afford immediate protection pending the development of resistance due to vaccination.

The authors have used an isoniazid-resistant BCG vaccine in newborn infants. The preparation of the vaccine and its properties are described by UNGAR *et al.* (*Brit. Med. J.* 1961, v. 1, 1498). [The abstract will appear in this *Bulletin*, 1961, v. 36, November.]

3 batches of freeze-dried vaccine were used; 2 were isoniazid-resistant with 8,800,000 and 4,900,000 viable organisms per 2 ml. respectively, and the 3rd was ordinary freeze-dried vaccine (8,000,000 viable organisms per 2 ml.). 3 groups of newborn infants were studied; they all received 0·1 ml. of vaccine intracutaneously.

60 infants of tuberculous mothers were isolated at birth, vaccinated with a resistant vaccine at once and given isoniazid 22 mgm. per kgm. daily. Mantoux tests with 100 TU of OT were done at intervals from the end of the 2nd post-vaccinal week until tuberculin conversion was demonstrated when the isoniazid was discontinued.

25 newborn infants were vaccinated with the ordinary vaccine and given isoniazid as above until tuberculin conversion occurred, but if this did not occur after 6 weeks the isoniazid was discontinued and the infant revaccinated.

The 3rd group consisted of 306 newborn infants of whom 107 were given the stronger resistant vaccine, 98 the weaker and 101 the ordinary vaccine. None was given isoniazid.

The results were analysed. 3 weeks after vaccination satisfactory tuberculin conversion was obtained with both batches of resistant vaccine; 1 infant who had received the stronger vaccine had to be revaccinated. The ordinary vaccine failed to produce conversion in 5 infants. The resistant vaccines both produced a slightly better conversion rate than the ordinary vaccine, and the inhibitory effect of the concurrent administration of isoniazid on conversion was seen in the infants receiving the non-resistant vaccine. The degree of tuberculin sensitivity present at 1 year and in the small number tested at 2 years was satisfactory. The authors recommend the use of the resistant vaccine wherever it is indicated. *H. G. Calwell*

Centro Per la Vaccinazione Antitubercolare in Toscana. La vaccinazione antitubercolare per multipuntura con il vaccino ucciso con formolo "anatubercolina integrale petragnani" (A.I.P.) alla luce di 10 anni di indagini sperimentali e di applicazione pratica. [**Vaccination against Tuberculosis by Multiple Puncture with Formol-Killed Vaccine "Anatubercolina Integrale Petragnani" (AIP). Results of 10 Years' Experimental Investigations and Practical Application**] *Ann. Sclavo.* Siena. 1961, v. 3, No. 1, Suppl., 48 pp., 15 figs. [33 refs.] English summary.

This long article by G. Mazzetti, G. Buonomini, L. F. Signorini, and G. Santopadre reports their own work and that of many concerned in an extensive campaign.

Petragnani's integral anatuberculin [AIP], first described in 1926, consists of a formol-killed suspension of 33 strains of *Myco. tuberculosis* of human, bovine and avian origin grown on Sauton medium. The final concentration is such that it is equal to a suspension of 3 mgm. of killed tubercle bacilli per ml. In a table, reproduced from Petragnani, in which AIP is compared with a human attenuated strain the effect, after inoculation, on the allergic state is given as +++ compared with ++++, and guineapig survival after challenge as 81·8% compared with 88·8%. Salvioli has used it on the newborn since 1932, giving intradermally on the medial aspect of the forearm a dose of 0·5 ml., equal to 1·5 mgm. of bacilli, distributing it at 4 points to avoid an excessive reaction. A satisfactory level of resistance is said to have been obtained, as judged by incidence in vaccinated contacts.

AIP intradermally produces a lesion of the tuberculous granuloma type, with the significance of a vaccinal focus, the injected bacteria disintegrating slowly. This focus "persists for months with phases of reactivation" [abstracter's translation]. Besides a change in the tuberculin reaction there is also a swing to positive with the complement-fixation test and with the Middlebrook-Dubos reaction.

As with other killed vaccines a fairly large dose was necessary, which must however not be so large that a strong local reaction will cause it to be rejected by the body. Scarification was not found effective, but the multiple puncture method was found to be the best in guineapigs even though the actual dose injected might be less than that which would have been given intradermally. Repeated inoculation by multiple puncture showed, through the appearance of a reaction of a Koch phenomenon type, that even where there had been no change in the skin tuberculin reaction, there had been produced an allergy to the bacilli, indicating an effective immunizing stimulus. On the basis of such findings the method was widely applied in man with the apparatus devised by Birkhaug [this *Bulletin*, 1948, v. 23, 23], on the deltoid region. The AIP was used as a paste (referred to as AIP-C, "C" standing for "concentrated") consisting of 60 parts by weight (moist) of tubercle bacilli and 40 parts of a 46·6% solution of polivynylpyrrolidone (known commercially as Subtosan). When it dries this leaves a thin protective film which renders further protection unnecessary. One application does not produce more than 50% tuberculin conversion; a second 3 to 6 months later raises this to 75 to 80%. Changes in the strength of the vaccine do not make any substantial difference. Administration by mouth in guineapigs was a failure even when given in 12 weekly doses and together with bile and hyaluronidase. Repeating the vaccine increases the effectiveness of AIP to a level attained by a lesser number of BCG administrations. Increasing the dosage alone does not improve results.

AIP induces immunity more slowly than BCG. A difference in survival time in guineapigs is only noticeable if the animals are challenged more than 100 days after vaccination, and only reaches statistically significant figures when there is a 6-month interval. When the interval is 60 days there is no protective effect, even though the animal is tuberculin positive. It is important that the challenge dose should be neither so small that the development of infection is too prolonged nor so large that control animals will succumb before lesions develop and thus confuse the issue.

The authors maintain that, unlike BCG, one dose of AIP-C, and sometimes even two, does not generally lead to a positive tuberculin reaction, but that an allergic sensitivity to the bacilli is constantly produced, as shown by the Koch phenomenon. This appears earlier and lasts longer. Reinoculation of a minimal dose of killed vaccine will produce the reappearance of allergy to tuberculin in animals in which it had disappeared (the Baldwin-Gardner-Willis-Saye phenomenon). Bacillary allergy is a clearer indication of immunity than sensitization to tuberculin. The immunizing power of a vaccine appears to be bound up with the structural integrity of the bacterial cell, though under experimental conditions disintegrated bacilli did protect.

The use of formalin as a killing agent has advantages over heat, such a vaccine keeping very well. Even AIP prepared 18 years before still ensured the survival of 75% of guineapigs when 50% of controls had died. In the same experiment 9-year-old AIP gave 83% survival and 1-year-old 91% (12 guineapigs were used in each of these groups). It is necessary to test each batch of vaccine (though not for sterility which is undertaken by the supplying institution). Not more than 20% of the bacteria must have lost their acid and alcohol fastness. Vaccine administered to a guineapig by 40 punctures over an area of 2 cm. in diameter must be capable of giving rise to a clear Koch phenomenon when a second application is given a month later.

Since 1950 AIP-C vaccination of tuberculin-negative subjects has been carried out by multiple puncture, most of the work being done in towns in Tuscany by a centre financed by the Ministry of Health and anti-tuberculosis associations of the province. After a propaganda campaign the scheme adopted made use of tuberculin testing, X-ray screening, followed by 2 inoculations at 3 to 6 months' interval and possibly a revaccination 3 to 4 years later, with continued

observation for several years. The subjects were mainly schoolchildren, of whom about 150,000 were tuberculin tested by a patch test. By 1958, 64,945 persons had been vaccinated. In the school year 1958–59 a review was made of children vaccinated in the preceding 5 years, 12,000 out of 54,000 being examined. In 5,719 originally tuberculin-negative children who had received 2 vaccinations there were 17 active and 87 inactive cases of tuberculosis; in 5,653 who had received 1 vaccination, 31 active and 156 inactive; in 3,818 tuberculin-negative untreated 22 active and 63 inactive; and in 3,873 originally tuberculin-positive untreated, 24 active and 221 inactive. As animal tests would have led one to anticipate, 1 vaccination was not useful. In fully vaccinated subjects incidence had been halved. The authors claim "a good success for a method which combines immunizing efficiency with ease of application and an absence of local and general incidents" [abstracter's translation]. Tuberculin-positive subjects showed 100% higher incidence of illness than those fully vaccinated, showing the insufficiency of natural "immunity".

The authors conclude that AIP-C behaves from the immunizing point of view just as BCG does. Experiments have shown that AIP-C produces a resistance which, after 3 weeks, inhibits the natural invasiveness of tubercle bacilli just as BCG does. [In spite of the authors' optimistic attitude, AIP seems from this report to have few advantages over BCG for an anti-tuberculosis campaign.] *E. Agius*

MOORE, P. E. **No Longer Captain: a History of Tuberculosis and its Control amongst Canadian Indians.** *Canadian Med. Ass. J.* 1961, May 6, v. 84, No. 18, 1012–16.

WYNN-WILLIAMS, N. **On Erythema Nodosum, Bilateral Hilar Lymphadenopathy and Sarcoidosis.** *Tubercle.* 1961, Mar., v. 42, No. 1, 57–63. [24 refs.]

190 patients suffering from erythema nodosum were seen at the Bedford General Hospital during the 10 years from 1949 to 1958. Of these 51 were children, 23 boys and 28 girls; 139 wer adults, 19 men and 120 women. An attempt was mad to classify the causes of the erythema nodosum; was thought to be tuberculous in 44, streptococcal i 51, uncertain in 48, due to drugs in 5 and BCG vac cination in 1 patient. In 41 it was considered to be manifestation of sarcoidosis. The condition wa thought to be one of tuberculous aetiology if a primar tuberculous lesion was present, or a tuberculous lesio developed within 1 year of the erythema nodosum, c if there was a history of close contact with a patien who had positive sputum on direct smear, an tuberculin test showed a high degree of sensitivity The cause was considered to be infection with beta haemolytic streptococcus if there was a definite histor of sore throat or if the anti-streptolysin titre was raised Sarcoidosis was diagnosed if there was bilateral hila enlargement, provided there was no lung shadow thought to be tuberculous and no history of clos contact in a patient having a high degree of tuberculi sensitivity. If no other cause was found and th patient had been treated with sulphonamide derivative during the preceding 2 weeks the condition wa diagnosed as being due to them.

Patients with erythema nodosum due to tuberculosi mostly showed a high degree of tuberculin sensi tivity. In the streptococcal and uncertain caus groups the tuberculin sensitivity figures were like thos of a similar healthy group in the area. Patients wit sarcoidosis on the other hand showed a lower degree of sensitivity than the other groups.

70 cases of bilateral hilar lymphadenopathy as manifestation of sarcoidosis were seen during the same decade. Of the 60 patients without pulmonary shadow in the first radiograph 40 had erythema nodosum, bu only one of the remaining 10 with pulmonary abnor malities had erythema nodosum. Just over one-hal of enlarged hilar gland nodes without pulmonary shadows had returned to normal size within 6 months and three-quarters within 1 year. 6 of the 70 patient developed widespread pulmonary changes while under observation, in 5 this was during the first year, bu in the 6th after 5 years.

Of the 60 patients who presented without pulmonary abnormalities, biopsies of one kind or another were done on 28; of these 10 showed positive sarcoi reactions. *F. H. Young*

VENEREAL DISEASES

COCKBURN, T. A. **The Origin of the Treponematoses.** *Bull. World Health Organization.* Geneva. 1961, v. 24, No. 2, 221–8.

This article is both philosophical and historical; it contains many facts and even more speculation.

Treponemata constitute species (defined as "groups of actually or potentially interbreeding natural populations which are reproductively isolated from other such groups"). All species of the genus *Treponema* must have been descended from one ancestral species. Isolation would interrupt interbreeding both geographically and ecologically. The former occurred when ice melted and water rose, separating large tracts of land which had previously been joined. All parasites are descended from free-living forms; symbiosis between them and the larger animals took place many million years ago Modern man appeared about 100,000 years ago

wandered over the world and took his parasites with him; both underwent adaptive changes in response to local conditions. After a long period various races would differ in their reactions to treponemes, and pinta is an example of the result of geographical isolation. By A.D. 1,000 treponemes could be commensals or parasites but owing to thinness of population, disease would be mild and chronic; as populations grew infections became more acute; one strain must have become venereal and syphilis as we know it appeared when a genitotropic strain had evolved. It is suggested that invasion of the internal organs is a result of congenital infection through a series of foetuses.

It seems that in the future the rate of spread of treponemes will increase and syphilis will be merely a mild infection of the mucous membranes of the sex organs.

[Only a few of the major points in this paper have been touched on; a study of the original should prove of absorbing interest to all who are interested in the history of syphilis.] *T. E. Osmond*

GRIN, E. I. **Endemic Treponematoses in the Sudan. A Report on a Survey.** *Bull. World Health Organization.* Geneva. 1961, v. 24, No. 2, 229–38, 2 figs. [11 refs.]

In 1959 a survey was carried out to discover the prevalence of (endemic) syphilis and yaws in the Sudan. In 1957–8, 141,980 cases of syphilis and 29,859 of yaws were diagnosed, compared with 122,685 and 41,819 in 1958–9; in 3 areas—Bahr el Ghazal, Equatoria, and Upper Nile—yaws predominated, while the reverse held in Darfur, Kassala, Khartoum, Kordofan and Northern Province; a large proportion of cases were in children; active clinical manifestations of yaws in children amounted to 43·1% of all examined or 95·6% of all early cases. In 3 villages surveyed in Equatoria the prevalence of active yaws was as high as 54%.

It was not always easy to distinguish endemic syphilis from yaws, in fact the two might co-exist in the same person; mucous lesions only exist where there is syphilis, they are not found in exclusively yaws areas.

In some areas syphilis is replacing yaws, and venereal syphilis introduced from the more urban parts is assuming the endemic non-venereal form owing to poor hygiene conditions prevailing in the villages.

It appears that some 5 million people in an area of 1,543,000 sq. km. are at risk and that about 20% of these suffer from active clinical treponematosis. Total mass treatment, which has been very effective in other places, seems definitely indicated.

T. E. Osmond

BENTZON, M. W. & KRAG, P. **The International Standard for Human Syphilitic Serum.** *Bull. World Health Organization.* Geneva. 1961, v. 24, No. 2, 257–64. [10 refs.]

This article is highly technical and as such does not lend itself well to abstraction: for details the original should be consulted.

For more than 40 years efforts have been made to find a method whereby different serum tests for syphilis carried out by different workers could be made to give comparable results. The League of Nations held 3 International Laboratory Congresses at which 20 different methods were used by serological specialists. In 1948 WHO approved an International Venereal Disease programme and reference standards were set up for cardiolipin and lecithin. [PANGBORN *et al.*, this *Bulletin*, 1952, v. 27, 52, WHO, *ibid.*, 1951, v. 21, 883; 1954, v. 29, 1086; 1959, v. 34, 471.]

The present paper sets out in great detail technical data for an International Standard for Human Syphilitic Serum. This serum is prepared in Copenhagen and consists of a pool of sera from 16 cases of syphilis in various stages, except primary; samples are freeze-dried, sealed under vacuum and stored at 4°C. or below: these are sent to laboratories as requested and can be used for assessing the sensitivity and specificity of the various methods employed in these laboratories. The international unit corresponds to 3·167 mgm. of the lyophilized specimen of serum. Examples are given of the techniques to be employed and of the calculations to be made.

In an annex is given a list of the 6 countries which participated in the collaborative assay and also of the 7 author-serologists who took part. *T. E. Osmond*

KRAG, P. & BENTZON, M. W. **The Third International Reference Preparation of Egg Lecithin.** *Bull. World Health Organization.* Geneva. 1961, v. 24, No. 2, 265–9. [12 refs.]

An international "reference" preparation of lecithin is essential if results of serum tests in different laboratories are to be comparable.

The first international preparation was established in 1951 and was replaced in 1953 by a second. This article reports on a third. An assay of this was undertaken in 1958 in 4 laboratories in 3 countries; for this purpose 32 reactive and 200 non-reactive sera were tested in parallel by using the new lecithin and a "reference" lecithin [WHO, this *Bulletin*, 1954, v. 29, 1086; 1959, v. 34, 471]. Detailed results are set out in the text and in 4 tables. Slide and complement-fixation tests showed only minor variations with reactive sera and all the non-reactive sera were completely negative. It was found that egg-lecithin in absolute alcohol in sealed ampoules kept well. This new preparation was found acceptable, having passed the chemical tests (phosphorous, nitrogen and iodine value) and having given comparable results with the "reference" preparation when combined with a reference preparation of cardiolipin and a good cholesterol; it is important for the assay to test both positive and negative sera and carry out tests on several days.

In order to produce sufficient egg-lecithin for 5–6 years 5,000 ml. were made and dissolved in absolute ethanol; this was found to withstand 56°C. for 14 days without appreciable loss of reactivity.

T. E. Osmond

ANDUJAR, J. J. & MAZUREK, Edith E. **Rapid and Small-Volume Reagin Tests.** *Bull. World Health Organization.* Geneva. 1961, v. 24, No. 2, 288–90. [10 refs.]

This article reports the results of Plasmocrit (PCT) tests [this *Bulletin*, 1959, v. 34, 884] on 17,623 specimens carried out in parallel with the VDRL test.

In a preliminary note the authors draw attention to the multiplicity of tests using treponemal antigens and point out that, in spite of these, reagin tests are still very much in the picture; plasma is superior to serum in tests for syphilis but it cannot be heated, and some other form of inactivation is therefore necessary; for this purpose choline chloride is suitable [*ibid.*, 1958, v. 33, 226]. The test is carried out on specimens collected in a capillary tube, which avoids venepuncture and enables an examination of red blood cells to be made on the same specimen—a procedure useful in industrial medicine. It is stressed that the PCT is essentially and only a screen test, useful in mass blood testing.

The specimens tested included 1,373 from syphilis patients, 7,831 from patients presumably free from syphilis and 8,419 from those whose syphilis status was unknown. Of the syphilitic subjects 53% were reactive with VDRL and 46% reactive with PCT: of the non-syphilitic subjects none were reactive with VDRL and 0·5% reactive with PCT.

The PCT appears occasionally to give prozone reactions, but this can be overcome by diluting the specimen 1/10: another serious drawback is that the choline-chloride antigen suspension sometimes shows an unpredictable drop in reactivity; however, this will be revealed if positive control specimens are included in every batch, as, of course, they should be; alternatively the disodium salt of ethylene-dinitrilo-tetra-acetic acid may be used to stabilize the emulsion [see also PORTNOY and GARSON, this *Bulletin*, 1961, v. 36, 357].

T. E. Osmond

VAISMAN, A. & HAMELIN, A. Valeur de la réaction de fixation du complément avec l'antigène *Treponema pallidum* ultrasoné pour le sérodiagnostic de la syphilis. [**Value of the Complement Fixation Test with *Treponema pallidum* Antigen Treated by Ultrasonic Waves in the Diagnosis of Syphilis**] *Bull. World Health Organization.* Geneva. 1961, v. 24, No. 2, 239–47. [21 refs.]

Following up the idea started by the use of Palligen and Pallignost and Reiter antigens these authors prepared one from the virulent Nichols strain of spirochaetes. Starting with the testicle of an infected rabbit they extracted this with normal saline centrifuged at 1,000 r.p.m. for 10 minutes to get rid of debris and then for 1 hour at 6,000 r.p.m.; the sediment was washed 4 times with saline, weighed and taken up in 0·3% phenol saline at 1 ml. per 50 mgm. of treponemes; it was then disintegrated by ultrasonic waves in an atmosphere of hydrogen in the cold. The suspension was then centrifuged at 6,000 r.p.m. for 15 minutes to clarify it. This suspension will keep indefinitely at 4°C.; for use it is diluted according to titration. For the complement-fixation reaction the Kolmer technique was adopted, with incubation at 6°C. for 18 hours followed by 10 minutes at 37°C.

6,000 sera and cerebrospinal fluids (CSF) were examined and 2,339 sera and 345 CSF tested by this test (TPCF) in parallel with the Kolmer CFT (cardiolipin), TPI, Kline, Kahn, and the Reiter (RPCF) tests. Of the sera all 4 tests agreed in 59%; of 856 sera positive with TPI, 727 were positive with TPCF, 621 with RPCF and only 150 with lipoid tests. Of 75 sera which were TPI negative but positive to classical tests [presumably false positives] TPCF was positive in 36 and RPCF in 53; of 24 sera from patients with primary syphilis negative with TPI and classical tests all were positive with RPCF and 9 with TPCF. Of the 345 CSF 273 were negative and 60 positive with all tests; of the 12 which gave discordant results all were positive with RPCF and TPCF, 6 were positive with TPI and 2 positive with WR. Further studies were carried out with rabbits, guineapigs and mice by injecting them with both live and dead spirochaetes.

The results are largely of academic interest; rabbits which developed clinical lesions behaved in much the same way as man in producing immobilizins and reagin; on the other hand guineapigs and mice which only develop asymptomatic syphilis produced the former but not the latter.

It is concluded that TPCF agrees most closely with TPI and shows satisfactory sensitivity and specificity. [However TPCF was positive in 36 out of 79 sera which were negative with TPI and positive with lipoid tests and could be regarded as false positives. In the English summary it is stated that TPCF antigen was prepared "from a *culture* [abstracter's italics] of pathogenic *T. pallidum*": this is obviously not correct if the word culture is used in its ordinary meaning.]

T. E. Osmond

MANNUCCI, E. & SPAGNOLI, U. La reazione di immuno-fluorescenza per la ricerca degli anticorpi della lue. (precisazioni di tecnica). [**Use of Fluorescent Immune Bodies in the Recognition of Syphilitic Antibodies**] *Ann. Sclavo.* Siena. 1961, Jan.–Feb., v. 3, No. 1, 49–62. 3 figs. (2 coloured on pl.). [20 refs.] English summary (8 lines).

The indirect method of COONS (*J. Immunology*, 1942, v. 45, 159) for recognizing antibody, *i.e.* the use of human antiglobulin conjugated with the isothiocyanate of fluorescein to reveal the coating of antigens with their corresponding antibody, has been employed to reveal the presence of antitreponemal immune bodies in human sera and hence to the diagnosis of syphilis.

This paper gives a detailed description of the technique required to give convincing results in such observations.

The Nichols strain of treponema was used to produce testicular lesions in the rabbit. The animals were killed on the seventh or eighth day and the testicles minced and extracted with rat embryo extract containing 5% of an ultra-filtrate of ox serum. A suspension containing 20–30 spirochaetes to each field of microscope at 500 magnifications is desirable.

The antiglobulin serum should have a titre of about 1–40,000 by the Coombs test of agglutination of red blood corpuscles coated with Rh antibody.

Conjugation of fluorescein isothiocyanate and antiglobulin is more successful with some samples than with others and the material should be used at the greatest dilution which gives frank results with a known positive syphilitic serum. The method of preparing the isothiocyanate of antiglobulin is described in great detail. A dilution of 1–50 of the serum under investigation for syphilitic antibody is recommended.

Fixation of treponema films is best with acetone and these are first left in contact with a 1–50 dilution of the serum under investigation for 30 minutes at 37°C. in a shaking apparatus under precautions to avoid too rapid drying. The films are then washed in buffer and treated with a drop of fluorescein antiglobulin in buffered 2% Tween 80.

The films are finally observed under direct white light to pick up the treponemata and then under ultraviolet light for fluorescence. A dry lens × 400–500 is recommended. Coloured plates of such preparations are included. In general the results correspond to those obtained by the method of treponema immobilization. *J. W. McLeod*

MAURY, P. H. & WEBER, A. Remarques à propos des résultats sérologiques obtenus dans la compagne de masse contre la syphilis au Maroc. [**Serological Tests in the Mass Campaign Against Syphilis in Morocco**] *Bull. World Health Organization.* Geneva. 1961, v. 24, No. 2, 281–7.

5 series of sera were examined from the areas El Kelaa, Taroudant, Rabat, Marrakesh and Casablanca in 1955–56. The percentages of reactive sera varied from 10 to 57; with the VDRL test doubtful results varied from 10 to 40%. Where the Kolmer test was carried out as well, 2% were positive with this and negative with VDRL. If treatment were undertaken on the strength of a doubtful VDRL 2–3% of the population would be treated uselessly. Malaria does not seem to have been a serious problem; it occurs mainly in small local epidemics and appears not to have affected serum tests to any great degree.

Numerous statistics are set out in 7 tables but do not appear to be of any great value beyond showing where positive sero-reactions were most numerous. [The standards of the various laboratories which carried out the tests do not seem to have been high; serum testing in the field is difficult. No clinical observations appear to have been made to confirm the results of serum tests.] *T. E. Osmond*

KALSTONE, B. M., HOWELL, J. A., Jr. & CLINE, F. X., Jr. **Granuloma Inguinale with Hematogenous Dissemination to the Spine.** *J. Amer. Med. Ass.* 1961, May 13, v. 176, No. 6, 530–32, 4 figs.

"Granuloma inguinale in a post-menopausal patient with hematogenous dissemination to the lumbar spine is a rare occurrence. Healing was affected in such a patient by chloramphenicol and spinal fusion."

[See this *Bulletin*, 1954, v. 29, 1050.]

LUDVÍK, J., STOKŁOSOVÁ, Stanislawa & WEGLARSKA, Barbara. Elektronmikroskopická a cytochemická studie *Trichomonas vaginalis.* [**Electron-Optical and Cytochemical Studies on *Trichomonas vaginalis***] *Československ. Parasit.* Prague. 1961, v. 8, 257–67, 5 figs. (4 on 4 pls.). [30 refs.] English summary.

BOYCOTT, J. A. **The Nature of Vaginal Discharge.** *Lancet.* 1961, May 20, 1071–4. [13 refs.]

"Of 561 specimens of vaginal discharge from women of reproductive age, 9 appeared to be due to bacterial infection. 134 were associated with *Trichomonas vaginalis*, and 64 with *Candida albicans*. The remainder were indistinguishable from normal vaginal secretion in any character except quantity.

"13/16 vaginal discharges in children and 15/18 in women over 50 appeared to be due to bacterial infection.

"A tentative classification of vaginal discharges based upon the reaction of the host and the parasite is suggested.

"It is possible that *C. albicans* is parasitic, not on the vaginal wall, but on the secretions of the vagina."

GENERAL INFECTIVE DISEASES

The order in this section is:—**General; Hospital and other Cross Infections; Coccal Infections; Bacterial Infections; Virus Infections.**

GENERAL

ZERBIB, P., DALOUS, A., SALANOVA, Jo & DEDIEU. Les vaccinations chez les enfants allergiques. [**Immunization of Infants Subject to Allergic Manifestations**] *J. Méd. de Bordeaux.* 1961, Apr., v. 138, No. 4, 564–8.

The authors, at a paediatric conference at Bordeaux in May 1960, discussed the problem of prophylactic vaccinations in allergic infants. They conclude that there is only one imperative contraindication to such vaccination. This is the case of anti-smallpox vaccination in the eczematous child.

This should never be done even when a slight manifestation of eczema is present, nor should an eczematous infant be allowed in contact with older children reacting to an inoculation of vaccine.

On the other hand a child showing asthmatic tendencies is especially in need of protection from pertussis

and should be inoculated with all due precautions, *i.e.* gradual desensitization with dilute preparations of the prophylactic at seasons in which asthma is usually in abeyance. *J. W. McLeod*

BAWA, Y. S. & WAHI, P. L. **Allergic Encephalomyelitis after Vaccination and Serum Therapy. Report of Ten Cases.** *Indian J. Med. Sci.* 1961, Apr., v. 15, No. 4, 290–97.

The authors give clinical details of 10 cases of neurological reactions to vaccine or serum therapy: 2 cases followed smallpox vaccination, 4 antirabic prophylaxis, 3 antitoxin therapy for clinical tetanus and 1 followed prophylactic anti-snake-venom. All the patients except 1 were treated with corticosteroids and the authors are satisfied that these had a beneficial effect on their patients. There is a brief discussion of the subject and references to the literature [this *Bulletin*, 1954, v. 29, 134, 912].

[The authors state that the cases were observed by them over a period of 2 years but the dates given show that 4 were seen in 1956, 2 in 1957, 2 in 1959, 1 in 1960 while 1 is undated: 1 of the cases dated back to 1952. The pathological diagnosis in some cases seems to rest on rather slender clinical grounds: 1 with wrist-drop and increased rigidity in the lower limbs following treatment for tetanus is diagnosed as transverse myelitis and radiculitis. Likewise recovery from the wrist drop after 6 weeks is regarded as marked improvement on corticosteroid therapy.] *A. B. Christie*

HOSPITAL AND OTHER CROSS INFECTIONS

ANDERSON, K. F., COULTER, J. R. & KEYNES, D. Ruth. **Staphylococcal Nasal Carriage in Mothers, Babies and Staff in a Maternity Hospital.** *J. Hygiene.* 1961, Mar., v. 59, No. 1, 15–27. [10 refs.]

407 mothers had their noses examined for *Staphylococcus aureus* before, during and after being in hospital for childbirth. 38% of the mothers were carriers before or at admission and 40% of their staphylococci were penicillin resistant. Nurses had the same carrier rate but 72% of the strains were penicillin resistant. A single swabbing failed to detect 25% of the people who would be shown as carriers by more frequent swabbing. The carrier rate was [according to the tables but not the text] slightly higher in the patients with a history of sepsis or who had been in hospital, but previous penicillin treatment was not associated with a higher causes rate for resistant strains.

Only 45% of the babies were carriers at discharge from hospital, usually about the 6th day. [This relatively early discharge may account for the low carrier rate.] 35% of the babies' strains were the same phage type as their mothers'; it is calculated that 36% were derived from other mothers and 29% from nursing staff. [The calculation is based on the relative rates of carriage of penicillin-resistant strains in mothers and nurses and does not utilize phage-typing results; it ignores the possibility that some babies are infected from other babies.] No difference could be detected between different phage types of staphylococci and their ease of transmission.

There was very little staphylococcal sepsis during the babies' hospital stay but 57 cases occurred in the following 6 weeks. Of 8 breast abscesses 6 were due to staphylococci carried by the mothers before admission; 7 were type 80/81; and in only 4 cases was the baby a nasal carrier. *R. E. O. Williams*

ELIAS-JONES, T. F., GORDON, I. & WHITTAKER, L. **Staphylococcal Infection of the Newborn in Hospital and in Domiciliary Practice.** *Lancet.* 1961, Mar. 18, 571–4. [21 refs.]

The staphylococcal sepsis rate in infants born in hospital in Ilford, Essex, was compared with that of infants born at home. 1,551 infants, the majority of whom were between 10 and 21 days old, were visited by the health visitor. When sepsis was noted, nose, umbilical and lesion swabs were taken and a comparable healthy infant, from whom nose and umbilical swabs were taken, was selected to serve as a control.

Of the 1,129 infants born in hospital 13·6% had septic lesions compared with 4·8% of infants born at home. Incidence was not seasonal and there appeared to be no correlation between sepsis rate and size of family, home conditions or obstetrical complications. 13·2% boys had lesions compared with 9·0% of girls but this was thought to reflect the sex difference in neonatal morbidity rates from all diseases. Sepsis was usually minor (conjunctivitis, skin lesions, umbilical infections).

The staphylococcal carriage rate was 77·5% in infants who developed sepsis compared with 50% in healthy controls. 71% infants born in hospital and 40·5% infants born at home were carriers but 90% of all the antibiotic-resistant strains found were from hospital born infants.

The authors make a plea for the abolition of communal nurseries and suggest that the practice of hospital confinement followed by lying-in at home, has much to commend it. *M. Patricia Jevons*

ZUPANC, E. **Control of a Staph Epidemic in a Small Nursery. Outbreak of Staphylococcal Infection among Newborn in a Small Hospital.** *Amer. J. Dis. Children.* 1961, Apr., v. 101, No. 4, 434–41, 1 fig. [24 refs.]

PLUECKHAHN, V. D. & BANKS, Joan. **Innocence and the Staphylococcus.** *Australasian Ann. of Med.* 1961, Feb., v. 10, No. 1, 59–67, 3 figs. [26 refs.]

This paper reports a study of staphylococcal infection in a district maternity hospital in Victoria, Australia, over 3½ years, during which time there were abou

2,400 deliveries per year. Daily inspection of the babies revealed skin or other sepsis in 19·7%; the rate had been as high as 41% in 1956 but fell to about 12% by the end of the study. There was no corresponding decline in the proportion of babies carrying staphylococci at the time of discharge. Of 8,473 babies, 31 were readmitted to hospital with serious staphylococcal disease later, and 8 died. 1·3% of 7,438 mothers developed breast abscesses. Type 80/81 was found but only accounted for about 12% of the babies' infection; Group III strains were common.

The improvement in the sepsis rates over the years is attributed first to improvement in aseptic routines generally [PLUECKHAHN and BANKS, this *Bulletin*, 1958, v. 33, 986], to minimizing skin and eye trauma, and to rooming-in. The incidence of sticky eyes was reduced when prophylaxis and "cleaning" of them was omitted.

R. E. O. Williams

FARRER, S. M., ZACHA, Elizabeth, CARVER, T. O., BENSON, W. W. & BARNEY, Louise. **An Epidemic of Staphylococcal Infections in a Mental Hospital.** *Amer. J. Pub. Health.* 1961, Apr., v. 51, No. 4, 556–65.

An epidemic of staphylococcal skin infections, mainly furuncles, pustules and impetiginous lesions, was observed among the adult patients and personnel of a mental hospital in Idaho. 63 of 658 patients were affected. The incidence was higher among males than females, and was highest in the youngest and oldest age-groups. 2 particular ward areas were heavily affected, the highest attack rate being in the medical-surgical block. Several phage types of staphylococci were isolated; the commonest was 52A/79. Only 1 type 80/81 strain was found. There was a possibility that infection was spread in some of the wards by staff with septic lesions. *R. E. O. Williams*

HOWE, C. W., SILVA, T. F., Jr., MARSTON, Alice T. & WOO, D. D. B. **Staphylococcal Contamination of Mattresses and Blankets on a Surgical Ward under Nonepidemic Conditions.** *New England J. of Med.* 1961, Mar. 30, v. 264, No. 13, 625–32, 1 fig. [12 refs.]

A large number of sweep-plate samples were taken from mattresses and blankets in a surgical ward and examined for staphylococci. The mattresses had, while in use, a plastic cover which was swabbed with phenolic detergent after each patient's discharge; after use by an infected patient they were fumigated with "cyanogen chloride." Blankets were routinely laundered each summer and "as far as possible after each patient is discharged."

Staph. aureus was isolated from only 2 of 512 cultures from mattresses but from 108 (46·1%) of 234 blanket cultures. The proportion of positive blankets increased from 5% of those sampled early in the period of use to 76% of those sampled after 3 months' use. Most positive blankets yielded 10 or fewer colonies of *Staph. aureus* per plate. 22% of the blankets yielded staphylococci with a phage type in the 52/52A/80/81/82 group; this was also the commonest type harboured by ward staff.

76 patients with clean operations were examined for a relationship between staphylococcal carriage and blanket contamination but no significant correlation could be found. Nor could any evidence be obtained of infection of wounds from blankets. Of 200 cultures from the bedding of patients with discharging staphylococcal lesions, 19 yielded *Staph. aureus*, in 9 cases of the same type as that from the lesion.

R. E. O. Williams

FOLEY, J. F., GRAVELLE, C. R., ENGLEHARD, W. E. & CHIN, T. D. Y. **Achromobacter Septicemia—Fatalities in Prematures. I. Clinical and Epidemiological Study.** *Amer. J. Dis. Children.* 1961, Mar., v. 101, No. 3, 279–88, 1 coloured fig. on pl.

During a 3-month period 6 infants died in a hospital in Nebraska; 4 of them yielded, from blood taken before or after death, a Gram-negative bacillus thought to belong to the *Achromobacter* group. All but 1 of the infants were premature, and only 1 had not had respiratory difficulty requiring treatment in an incubator. The clinical signs of the infection included cyanosis, lethargy, periods of apnoea and failure to feed. All the infants developed a distinctive rash: an area of erythematous induration with a well developed margin, usually commencing on the cheek and extending rapidly over the head, neck, arms and upper part of the chest. Death usually occurred 2 days after the appearance of the rash.

Many bacteriological examinations were made of healthy babies, personnel and environment, but bacilli resembling those from the sick infants were found only in the respiratory tract of 4 infants, in the humidifying water of an incubator and in a bottle of water used for washing the infants' eyes. The organism is a motile Gram-negative bacillus which, at 37°C., ferments no sugars and gives negative indole, methyl red and acetyl methyl carbinol tests. A specific agglutinating serum was prepared.

Examination revealed many defects in the hygienic precautions adopted in the nursery. After cleaning and disinfection of the nursery and improvements in asepsis no further cases of infection were seen.

R. E. O. Williams

CABRERA, H. A. & DAVIS, G. H. **Epidemic Meningitis of the Newborn caused by Flavobacteria. I. Epidemiology and Bacteriology.** *Amer. J. Dis. Children.* 1961, Mar., v. 101, No. 3, 289–95, 2 figs.

GEORGE, R. M., COCHRAN, C. P. & WHEELER, W. E. **II. Clinical Manifestations and Treatment.** *Ibid.*, 296–304, 1 fig.

I. In a maternity nursery outbreak there were 14 cases of meningitis due to a Gram-negative bacillus identified as *Flavobacterium meningosepticum* [see KING,

this *Bulletin*, 1959, v. 34, 1182]; 10 infants died, and of the 4 who recovered 3 had hydrocephalus. 30 infants without symptoms were found to be colonized by the same organism, but carriage was never persistent after erythromycin treatment. No carriers were found among the staff but the bacilli were recovered from a sink trap in the nursery and from the handle of a hamper. It was thought that the organism was most probably transmitted by hands, possibly from bottles contaminated by the faulty sink trap.

II. The clinical picture did not differ from that of other bacterial meningitis of the newborn. 3 of the 14 babies died, apparently from toxaemia, very early in their illness, but all had microscopic evidence of meningitis. 5 infants developed a fatal necrotizing meningitis, starting between about the 3rd and 9th day of life. 4 infants survived the meningitis but developed hydrocephalus. 1 child had a pneumonia and one with meningitis leading to hydrocephalus was only diagnosed serologically.

The cerebrospinal fluid showed very large numbers of bacilli in stained preparations with, on average, about 1,300 leucocytes per cmm. Only erythromycin, oleandomycin, ristocetin and vancomycin inhibited the growth of cultures; antibiotic treatment of the illness was ineffective.

The flavobacteria from the patients grew in the smooth form and carried an antigen lacking in ordinary environmental strains of similar organisms. Although perhaps these organisms are not readily able to invade the tissues, such invasion when it occurred was followed by very severe damage to the central nervous system. Surviving infants developed specific antibodies.

[An Editorial in the same number of the journal ("Water Bugs in the Bassinet") comments on this paper and the paper by FOLEY *et al.* (p. 899) and presents a brief review of the literature.] *R. E. O. Williams*

COCCAL INFECTIONS

The order in this section is:—***Staphylococcus, Streptococcus, Neisseria, Others.***

CORLETT, K. **Staphylococcal Septicaemia with Ulcerative Endocarditis, successfully treated with Celbenin.** *New Zealand Med. J.* 1961, Mar., v. 60, No. 343, 112–13, 1 chart.

"A case of staphylococcal septicaemia complicated by acute endocarditis is described which failed to respond, despite apparent sensitivity to most antibiotics. There was a dramatic response to celbenin B.R.L. 1241."

BLACK, P. H., SWARTZ, M. N., SHARP, J. T., KUNZ, L. J., STOKES, J., III. & MCFARLAND, R. B. **Severe Streptococcal Disease. Observations during an Epidemic occurring in Southern New England, 1958–1959.** *New England J. of Med.* 1961, May 4, v. 264, No. 18, 898–903, 1 fig. [25 refs.]

The authors report that the incidence of streptococcal infection has been rising in the U.S.A. and that the figures for 1959 were 3·5 times those of 1947. In 1959 an epidemic of streptococcal infection occurred in Southern New England and the authors here give some facts referring to 174 patients treated in the Massachusetts General Hospital; 92 had pharyngitis and 56 cellulitis. 5 died from varying forms of infection—1 was over 80 years old, 2 over 60, 1 was 46 and 1 was 18 days old: all were rapidly fatal in spite of large doses of penicillin. Penicillin remains, however, the best antibiotic for streptococcal infections. The authors draw attention to the epidemiological differences to be expected in military and civil communities.

A. B. Christie

ARDELEAN, I., BALDOVIN-AGAPI, Coralia, IENIŞTEA, C., PETRESCO, Ana M., DUMITRESCO, V., PAŞOLESCO, Ortansa, GRIGORIU, T., PTEANCO, A., KLEIN, R., NEGRU, Florica & VASILIU, Ecaterina. Observations sur les porteurs de streptocoques hémolytiques, dans des collectivités d'enfants, à caractéristiques épidémiologiques variées. [**Observations concerning Carriers of Haemolytic Streptococci in Children's Communities exhibiting various Epidemiological Characteristics**] *Arch. Roumaines Path. Expér. et Microbiol.* 1960, Dec., v. 19, No. 4, 527–39, 1 graph.

Throat cultures from children in 2 towns and 1 village in Rumania were examined monthly during 1 school year for the presence of haemolytic streptococci. A total of 601 children yielded 4,598 cultures of which 835 showed the presence of haemolytic streptococci. 370 of the strains belonged to group A, giving a *Streptococcus pyogenes* carrier rate of 8·1%. There were no notable differences between the different population groups, nor was there any consistent seasonal change. Type 8/25 constituted 46% of the group A strains, type 2, 17%, and type 12, 11%. 72% of the children yielded haemolytic streptococci from one or more cultures. A number of persistent carriers were observed. *R. E. O. Williams*

HALL, P. **On the Prognosis and Natural History of Acute Rheumatic Fever and Rheumatic Heart Disease. A Study based upon a 25-Year Material in a Swedish Town served by a Single Hospital.** *Acta Med. Scandinavica.* 1961, v. 169, Suppl. 362, 122 pp., 42 figs. [Numerous refs.]

Malmö is a town of just over 200,000 population. Apart from one small paediatric clinic it is served by one hospital only. It seemed therefore an ideal town in which to review the incidence of one disease in a population. All cases of acute rheumatic fever and rheumatic heart disease treated in the hospital between 1930 and 1954 are surveyed in an attempt to study the natural history of the conditions in a given population over a long period. The monograph is in two parts

part I relating to acute rheumatic fever and part II to rheumatic heart disease.

In each section the literature of the condition is first reviewed and the basis of diagnosis for each condition established. The material available from the Malmö records is then analysed in detail, the diagnoses of acute rheumatic fever being classified as " firm," " probable " and " suspected ". The experience of the patients over the 25-year period is assessed and an attempt is made to estimate the incidence, prevalence and severity of the conditions throughout the period and to relate the findings in Malmö to those reported in the literature. At the end of each part the findings are given as being in agreement with or differing from the reported findings.

With regard to acute rheumatic fever the main findings in agreement with the literature were that the frequency of the disease was decreasing, that acute mortality was low and decreasing, that patients with a first attack at age over 30 rarely developed heart disease, that 40% of recurrences occurred within 2 years of first attack and 80% within 10 years and that recurrences were rare in patients whose first attack occurred after 30 years of age. Findings in disagreement with the literature were that the age of onset of the group with polyarthritis was high (mean age 25 years) and also in the group with acute endocarditis (17 years) and that all manifestations increased during the war years. The main finding with regard to frequency was that the disease was decreasing and the decrease was most marked after 1950. The main findings with regard to rheumatic heart disease were in agreement with reports of previous investigations: differences related mainly to age at onset of various symptoms. [There is a great deal of material in this monograph, including an analysis of 88 operations for mitral stenosis, which cannot be adequately abstracted. It is especially of interest to physicians interested in the prognosis of rheumatic fever but is also recommended as an exercise in social medicine.] *A. B. Christie*

Bywaters, E. G. L. & Thomas, G. T. **Bed Rest, Salicylates, and Steroid in Rheumatic Fever.** *Brit. Med. J.* 1961, June 10, 1628–34, 5 figs. [15 refs.]

The authors in 1948–50 treated 139 patients with rheumatic fever by bed-rest supplemented only by analgesics to control pain, but without salicylates or steroids. In 1950–1 they treated 86 patients with 6-week courses of salicylates, cortisone or corticotrophin [this *Bulletin*, 1955, v. 30, 868]. A third group of 47 patients were subsequently treated with 12-week courses of cortisone or salicylates. The authors' conclusions are that for the majority of patients, bed-rest gives as good results as the other treatments: that salicylates relieve symptoms but do not affect the incidence of cardiac complications: that steroids may shorten the duration of rheumatic activity but do not benefit the heart except perhaps in the development or disappearance of soft systolic murmurs, a factor which in any case does not appear to affect cardiac status after 5 years. Steroids should be used in all patients with cardiac enlargement and marked activity: they may prevent cardiac failure or when it is present allow a satisfactory response to digitalis or massage. Salicylates on the other hand may in such cases be dangerous, precipitating lung oedema or rheumatic pneumonia. *A. B. Christie*

Thomas, G. T. **Five-Year Follow-Up on Patients with Rheumatic Fever treated by Bed Rest, Steroids, or Salicylate.** *Brit. Med. J.* 1961, June 10, 1635–9.

The author treated and followed for 5–10 years 125 patients with bed-rest only and 73 with 6-week courses of salicylates, cortisone or corticotrophin. The bed-rest patients were given no prophylaxis, but the others had 1 gm. sulphonamide daily while in hospital and during the follow-up period. 174 patients had no recurrences and among these there were no differences as regards cardiac status between the bed-rest group and the treated group. In the bed-rest group there were 19 recurrences (15%): in 7 patients cardiac signs increased and 2 patients died. In the treated group there were 5 recurrences (6·8%) and no patients deteriorated. The author concludes that steroids and salicylates have little effect in most cases on cardiac status as observed at follow-up, but that specific prophylaxis, in this case with sulphonamides, is the most certain way of reducing cardiac complications and mortality in rheumatic fever. *A. B. Christie*

Dorfman, A., Gross, J. I. & Lorincz, A. E. **The Treatment of Acute Rheumatic Fever.** *Pediatrics.* Springfield, Ill. 1961, May, v. 27, No. 5, Pt. 1, 692–706, 6 figs. [36 refs.]

131 patients suffering from acute rheumatic fever were given a basic treatment consisting of 15 weeks' bed-rest, initial high dosage of penicillin followed by maintenance sulphonamide dosage, and regulated amounts of potassium chloride and sodium chloride. 1 group was given nothing else, 1 corticosteroids, 1 salicylates and 1 a combination of the 2 drugs. Treatment with corticosteroids resulted in a decrease in apical systolic murmurs at the end of a year but there was no obvious advantage in combined treatment. When there is evidence of carditis, corticosteroids in a dosage equivalent to 2 mgm. per kgm. hydrocortisone for 9 weeks with reduction after that time should be given. When there is no evidence of carditis, salicylates sufficient to maintain a blood level of 20 to 30 mgm. per 100 ml. of blood are suitable. The basic treatment is essential to all. *A. B. Christie*

Feinstein, A. R. **Standards, Stethoscopes Steroids and Statistics. The Problem of Evaluating Treatment in Acute Rheumatic Fever.** *Pediatrics.* Springfield, Ill. 1961, May, v. 27, No. 5, Pt. 1, 819–28. [48 refs.]

The author lists 10 different recommendations for the treatment of acute rheumatic fever drawn from published reports of well-known investigators. He then

analyses the causes of the differences and shows that these are due not to differing therapeutic effects but to the inclusion in compared groups of different percentages of patients with different cardiac prognoses. He discusses the factors affecting the classification of patients and, in tables, shows to what extent the investigators have paid attention to them. [A refreshing approach to a confused subject.] *A. B. Christie*

ROEMER, G. B. & MAI, K. Antikörpernachweis bei Enterokokken-Infektionen des Menschen durch indirekte Hämagglutination. **[Demonstration of Antibodies in Enterococcus Infection in Man by Indirect Haemagglutination]** *Ztschr. f. Hyg. u. Infektionskr.* 1960, v. 147, No. 2, 109–22. [13 refs.]

Human erythrocytes were sensitized with a formamide extract of a standard enterococcus strain; they were then used to titrate the antibody in a series of human sera. Of 500 normal sera only 7 gave agglutination in a dilution of 1/32 or more; only 2 gave titres of 1/64 or more. Details are presented of 5 patients proved to have Group D streptococcus infection; 1 had a serum haemagglutination titre of over 1/1,000 (which decreased as the infection was brought under control); the others all had titres of 1/64 or more. The serum from the first patient also showed precipitation with a group D extract; absorption with the extract lowered the haemagglutination titre somewhat. *R. E. O. Williams*

HARVEY, H. S. & DUNLAP, Marjorie B. **Seasonal Prevalence of Upper Respiratory Pathogens.** *New England J. of Med.* 1961, Apr. 6, v. 264, No. 14, 684–6, 3 figs.

The prevalence of common potential respiratory pathogens was studied over a period of 7 years in 97 healthy families [this *Bulletin*, 1957, v. 32, 476; 1960, v. 35, 1200] in order to ascertain whether there existed an increased seasonal incidence of any particular organism, or group of organisms, in the upper respiratory flora. Cultures were taken every month from each member of the family, the total number of cultures being approximately 100 per month. The organisms involved were the streptococcus, *Haemophilus influenzae* and the pneumococcus.

It was found that the incidence of each of these individual organisms did not run parallel and only rarely did one organism reach a peak coincident with one of the other organisms reaching a low point. Neither did the occurrence of one species of organism in a person mutually exclude the presence of any of the other 2, it having been shown conclusively over the 7-year study that in any one person all 3 may be present in the same culture.

With regard to the prevalence of the individual organisms, the scores for the *H. influenzae* were somewhat higher because of its more general presence. Those for the pneumococcus were higher in the noses than in the throats of young children and babies; and the incidence persisted throughout summer and early autumn. The incidence of streptococci was found not always to run parallel to the seasonal increase in streptococcal disease. Remarkably, the lowest score for the streptococcus was obtained in November, 1957, at the height of the Asian influenza epidemic, when the reverse would have been expected.

Overall the findings were that the expected increase in potential pathogens during winter and spring did not in fact always take place and that the highest peak was sometimes reached in summer.

It would thus appear that the incidence of potential upper respiratory pathogens does not in fact correspond with the increase in the incidence of upper respiratory disease. This suggests that other seasonal factors prevail which are not explicable in terms of bacterial flora. *Robert L. C. Cumming*

ESRACHOWITZ, Sheila R. **The Treatment of Pyogenic Meningitis—is Intrathecal Therapy Necessary?** *South African Med. J.* 1961, Apr. 8, v. 35, No. 14, 281–3.

The author treated 71 cases of pyogenic meningitis in young children with combined chloramphenicol and sulphonamides: penicillin or streptomycin was added when the response was poor. 28 patients were also given 250 μgm. of chloramphenicol intrathecally: this dose was intended to be given daily until the cerebrospinal fluid had a normal sugar content and did not contain more than 40–50 cells per ml. but it was not quite clear whether in fact this routine was adhered to, owing to difficulty of preparing intrathecal chloramphenicol. The survival rates in pneumococcal and *Haemophilus influenzae* meningitis—the largest group—were 77% with intrathecal and 78% without intrathecal therapy: survivors classified as "well" were 59% with and 71% without intrathecal therapy. When all forms of pyogenic meningitis were included, the survival rates were 71% with and 86% without intrathecal therapy and the "well" rates 57% and 74%. When discussing the comparability of the 2 groups, the author makes the rather surprising statement that "apart from the greater incidence of fits and depressed level of consciousness, the IT [intrathecal] group were at no disadvantage": the percentage of children with depressed level of consciousness on admission was 54% in the intrathecal group against 21% in the other, and with fits before admission 50% against 28%. The author concludes that "any benefit derived from injection of drugs into the theca is very doubtful". [This may well be true, but the author's figures refer solely to a rather severe and prolonged course of intrathecal injections of chloramphenicol, mainly in pneumococcal and *H. influenzae* meningitis]. *A. B. Christie*

BACTERIAL INFECTIONS

The order in this section is:—***General, Corynebacterium, Haemophilus, Enteric bacteria, Brucella, Pasteurella, Bacillus, Anaerobes, Spirochaetes, Others.***

BONZANO, L. Una epidemia di difterite in Biella e circondario. [**An Epidemic of Diphtheria in Biella and its Surroundings**] *Giorn. di Malattie Infettive e Parassit.* 1961, Feb., v. 13, No. 2, 112–15, 1 graph. [25 refs.]

Into the isolation wards of the hospital of Biella [a wood manufacturing centre in Piedmont] 134 children, in the first 12 years of life, were admitted with diphtheria between October 1958 and October 1959. 63 of the patients came from the town itself, the remainder were from surrounding districts. 52 patients, nearly 39%, were aged 6–8 years. 89, over 66%, had received anti-diphtheria inoculations and 3 of these children were among the 4 who died.

The localization was in the pharynx in the majority of cases, as shown in a table which gives details of this and of complications, which were as high as 30%; these seemed to be less serious in those who had been immunized and their frequency seemed to be in direct proportion to the interval which had elapsed since inoculation. Among those immunized, the highest incidence of infection appeared within 2 years of inoculation.

In spite of immunization, diphtheria still prevails and causes considerable mortality in Italy, and various factors have been adduced, and are quoted by Bonzano, to explain why this is so. He considers that a repeat dose of vaccine should be given every other year.

J. Cauchi

MEHTA, O. N. **Schick Test in Ludhiana District.** *J. Indian Med. Ass.* 1961, Mar. 16, v. 36, No. 6, 231–4.

Mass immunization against diphtheria of schoolchildren in the Punjab has been advocated but as the exact incidence of diphtheria is unknown for reasons which are here detailed, it was considered to be advisable to obtain evidence of the degree of susceptibility or immunity to the disease by means of Schick testing before embarking on an extensive and costly campaign of immunization.

1,805 children from urban and rural areas of ages ranging from 1 to 11 years were selected for Schick testing. Among the main results it was found that (1) in 521 pre-school children 1 to 6 years of age the Schick positive percentage was 22·2% at 1 to 2 years diminishing steadily to 10·2% at 5 to 6 years. In the girls the rate was higher than in boys and (2) in 1,284 schoolchildren the Schick positive rate in 657 aged 6–7 years was 6·3% and in 627 aged 10–11 years was 3·6%. A comparison of the figures for urban and rural schoolchildren showed that at 6–7 years of age the positive rate was about the same in the 2 groups but at 10–11 years the Schick positive rates in the urban areas were 3·8% for boys and 6·6% for girls but in the rural areas 1·6% for boys and 3·8% for girls.

The opinion formed on this evidence is that there appears to be hardly any justification for carrying out diphtheria immunization in the schoolchildren but that there is an indication for immunization at 1–5 years which can be carried out through the maternity and child welfare and primary health centres which are being opened throughout the country.

M. E. Delafield

BOKKENHEUSER, V. & STEPHEN, A. **Diphtheria in Durban: Morbidity, Mortality and Prevention.** *South African Med. J.* 1961, Apr. 8, v. 35, No. 14, 289–94, 2 figs. [22 refs.]

Durban is a city of approximately half a million people, divided into 4 racial groups; White, Asian, Coloured, and Bantu. In the period 1940–58 the notification rate of diphtheria has dropped from 209·4 per 100,000 in 1944 to 20·1 in 1957, while the notification rate for the Union of South Africa as a whole has remained steady at a level of about 20–25 per 100,000. When the mean rates of 4-year periods were used to smooth out random fluctuations the notification rates were shown to have dropped in 3 racial groups: White from 272·38 in 1940–44 to 36·42 in 1955–58, Bantu from 65·70 to 39·61, and Coloured from 386·94 to 73·58; Asian rates have remained steady at 20·55 to 31·90.

The authors point out, however, that this is not the success story that it might appear to be. During these years the mean annual number of deaths (from diphtheria) notified did not decrease, varying from 4·82 per 100,000 in 1940–44 to 7·63 in 1950–54 and 5·55 in 1955–58. This of course means that on these figures the mortality rate was rising; in Whites from 1·87% in 1940–44 to 5·85% in 1954–58, in Asians from 7·25% to 19·47%, in the Coloured people from 1·94% to 5·4% and in the Bantu from 13·11% to 20·42%.

They then discuss the possible explanations of these figures. The degree of immunization could only be ascertained adequately for the White group. In these the rate of immunization carried out below the age of 2 years rose from under 25% in the present 15–19 age-group to just over 70% in the 1–4 age group. This might account for the lower incidence but not for the higher mortality.

There was no evidence of enhanced pathogenicity of infecting strains, the probable percentage of *mitis* type being 90%. In any case this would not explain the wide variations in racial mortality. Delay in treatment might explain some of the increase, but the maximal mortality experienced with *mitis* strains was 10% after 4–5 days delay. Lower resistance was considered, but not regarded as an adequate explanation.

Finally the authors advance the hypothesis that increasing inadequacy of notification, particularly among the Bantu, is the true reason for the lower notification rates with the higher mortality rates. They suggest that only approximately 1 in 3 of the Bantu cases are notified.

Accepting this hypothesis they present corrected estimates of the incidence in the different years and in the different racial groups based on the mortality figures and on probable mortality rates. These figures are much higher, particularly in the Bantu, and do not show much improvement, except in the Whites where it may be associated with increased immunization [see also this *Bulletin*, 1961, v. 36, 365]. *A. C. E. Cole*

BHATT, A. N. & BHARFAVA, H. S. **Laryngeal Diphtheria. A Study of 56 Cases.** *Indian J. Med. Sci.* 1960, Sept., v. 14, No. 9, 793–800, 5 figs.

56 patients with laryngeal diphtheria in Nagpur, India, were treated in 1957–58 with penicillin and antitoxin with or without tracheotomy. Only 2 patients had no membrane on the throat and 22 had severe toxaemia. 26 of the patients died (46·4%), 15 after tracheotomy. The authors estimate that at least 100,000 children die annually in India from laryngeal diphtheria. [Most of the patients seem to have been suffering from combined laryngeal and pharyngeal diphtheria: in Britain, when diphtheria was common, the membrane in laryngeal diphtheria was usually confined to the larynx.]
A. B. Christie

FUNT, T. R. **Primary Cutaneous Diphtheria.** *J. Amer. Med. Ass.* 1961, Apr. 29, v. 176, No. 4, 273–5. [17 refs.]

A pustule on the shoulder of a 30-year-old man developed in 10 days into a deep ulcer, 3 cm. by 5 cm. in size. The patient appeared to be acutely ill, his temperature was 103°F. (39·4°C.) and he had some difficulty in speaking, giddiness and a staggering gait. 12 million units of penicillin were given intravenously in the first 24 hours with dramatic response in the general and local symptoms but when the dose was dropped to 6 million units there was recurrence of the general symptoms and the higher dose was recommenced. Smears from the ulcer showed organisms resembling *Corynebacterium diphtheriae* and culture confirmed that this was a virulent strain of *mitis* type. 30,000 units of diphtheria antitoxin were given but at what stage it is not clear. Recovery was complete without complications. The diagnoses considered were anthrax, diphtheria and tularaemia. There is a useful discussion on cutaneous diphtheria. *A. B. Christie*

KASZA, L. & CSOSZ, I. K. **Cortisone and Phenylbutazone in the Treatment of Diphtheritic Croup and Non-Diphtheritic Stenosing Laryngitis.** *Rumanian Med. Rev.* 1960, Oct.–Dec., v. 4, No. 4, 41–4.

The authors treated 63 patients suffering from laryngeal diphtheria with, in addition to penicillin and antitoxin, 50–100 mgm. of cortisone and (in 13 patients) 10 mgm./kgm. phenylbutazone also. These drugs were usually given once only, though in a few cases the cortisone was repeated for 2 or 3 days. The patients were treated between 1957 and 1960 and the effect of the treatment was assessed by comparing results of penicillin and antitoxin treatment given to 153 patients between 1950 and 1957. Of these 153, 31 required tracheotomy, of the 63 treated with cortisone and phenylbutazone only 4: there were 29 deaths in the earlier group compared with 1 only in the later. 20 patients with non-diphtheritic stenosing laryngitis were also treated with cortisone or phenylbutazone or both with satisfactory results. The authors could find no difference between patients given only cortisone in addition to antitoxin and antibiotics and those given both cortisone and phenylbutazone but they were satisfied that these drugs singly or together brought rapid relief to patients, reduced the need for tracheotomy and saved lives. *A. B. Christie*

PINTO, I. J., DESAI, A. J. & THANAWALLA, J. K. **Cardiac Problems in Diphtheria and their Management.** *J. of J.J. Group Hosps. & Grant Med. College.* Bombay. 1961, Apr., v. 6, No. 2, 133–41. [10 refs.]

This is a study of cardiac changes in 64 patients suffering from bull-neck diphtheria. The patients were divided into 3 groups according to the clinical and electrocardiographic evidence of severity. In the most severe grade, 9 of 11 patients died: these patients had incessant vomiting, marked oliguria, shock, gallop rhythm and Stokes-Adams syndrome along with gross ST segment changes and various grades of heart block shown in the electrocardiogram. In the second grade of severity, 5 of 33 patients died and in the first grade only 1 of 20. Of the 15 patients who died, 14 were under 5 years old. Treatment was disappointing and cortisone seemed to be of no avail: 40% of the cortisone-treated patients died, compared with 14% of the others, but cortisone was given only in the severer cases. *A. B. Christie*

VIRDIS, F. Un quindicennio di profilassi antidifterica nel Comune di Parma (1946–1960). **[Fifteen Years of Antidiphtherial Prophylaxis in the Commune of Parma]** *Igiene Moderna.* 1960, v. 53, Nos. 9/10, 563–9. English summary (7 lines).

In Parma since 1946, diphtheria vaccine has been given in 2 successive doses, at an interval of 3–4 weeks, during the second year of life, followed by a third dose 6 months later. Diphtheria is notifiable and the patients are isolated, and terminal disinfection is carried out. Bacteriological investigations are made and any carriers found are excluded from contact with their schoolfellows or their fellow-workers and given sterilizing drugs. If 2 years have elapsed since their last inoculation, children are given a booster dose before they are admitted to holiday camps. Children are examined for the carrier state if they are to go into children's homes or similar institutions.

The authors show in a table, for each of the 15 years, the Parma population figure, the number of inoculations and of notifications, the morbidity rate per 10,000 inhabitants and the corresponding rates for the whole

country. Up to 1957 the Parma rate has been consistently higher, some years many times higher, than for Italy as a whole. The Parma rate has been lower than the national rate for each of the years 1958–60. In the years 1949–55 the Parma rate ranged from 6·1 to 19·1 and the national rate from 2·45 to 3·30. Deficient immunization during and immediately after the war may have combined with housing shortage and unfavourable climatic and other factors to account for local high incidence of the disease. The last few years are showing the benefits, in the form of a much reduced incidence, derived from more effective immunization carried out over the preceding period. *J. Cauchi*

GROOVER, R. V., SUTHERLAND, J. M. & LANDING, B. H. **Purulent Meningitis of Newborn Infants. Eleven-Year Experience in the Antibiotic Era.** *New England J. of Med.* 1961, June 1, v. 264, No. 22, 1115–21, 1 fig. [27 refs.]

The authors review 39 cases of neonatal meningitis treated at the Children's Hospital and General Hospital, Cincinnati, between 1948 and 1959. *Escherichia coli* was the organism in 4 cases, haemolytic streptococci in 5, and *Paracolobactrum* in 7: other organisms were *Aerobacter* (2), *Klebsiella pneumoniae* (1), *Proteus* (1), *Haemophilus influenzae* (1) *Listeria monocytogenes* (3), *Staphylococcus albus* (1) and *Streptococcus pneumoniae* (1): in 13 cases the organism was unknown. Meningitis was commoner after obstetrical difficulties, and in premature babies the onset was earlier than in full-term babies. Symptoms were vague and varied and the diagnosis was often missed. The mortality was 66·6% in spite of the use of a variety of antibiotics.

A. B. Christie

JONES, D. M. M. & PANTIN, C. G. **Typhoid Voirrey. An Account of a Woman who was a Typhoid Carrier for more than Half a Century.** *Monthly Bull. Ministry of Health & Pub. Health Lab. Service (directed by Med. Res. Council).* 1961, Feb., v. 20, 20–27, 1 diagram.

This paper gives an account of a typhoid carrier who is presumed to have contracted typhoid fever in a small village in the Isle of Man round about the turn of the century and is believed to have been responsible for infecting a number of persons between then and 1932. The evidence since that date until recent years is more complete and between the period 1932 to 1955 no fewer than 22 cases of typhoid fever can be traced with some certainty to this particular carrier. *H. J. Bensted*

ROWLAND, H. A. K. **The Treatment of Typhoid Fever.** *J. Trop. Med. & Hyg.* 1961, May, v. 64, No. 5, 101–10.

This is a study of 520 patients suffering from typhoid fever and treated by 12 different schedules. Chloramphenicol was given in 6 different dosages with or without the addition of a 3-day course of prednisone. For a 70-kgm. patient the doses of chloramphenicol ranged from approximately 1 gm. every 6 hours for 5 days to 250 mgm. every 6 hours for 10 days: the dose of prednisone in each case was approximately 56 mgm. every 6 hours for 3 days. The patients were divided fairly evenly by number into the 12 treatment groups, though the authors point out that there were differences in the proportion of severe cases in the groups. The most important factor influencing prognosis was undoubtedly severity of illness on admission and this in turn depended on economic status and previous TAB inoculation. Mortality depended on the same factors and was also influenced by age, 12 of 18 deaths occurring in children under 10. No schedule stood out as superior to the others but total amount of chloramphenicol and length of treatment seemed to be relevant. Prednisone reduced temperature but did not otherwise seem to influence the prognosis. As far as conclusions can be drawn, the authors feel that for severely ill patients a 10-day course is better than a 5-day course but that in less severe cases the differences in results could have arisen by chance. [The article is difficult to abstract but is worth careful study in the original.]

A. B. Christie

STAGIRA, A. & MARINAZZO, A. Considerazioni su 50 casi di tifo addominale trattati con desametazone e con CAF. **[50 Cases of Typhoid Fever Treated with Dexamethasone and Chloramphenicol]** *Giorn. di Malattie Infettive e Parassit.* 1961, Feb., v. 13, No. 2, 116–17.

The authors here report on the treatment of 29 men and 21 women, aged 9–45 years; the majority were admitted about the end of the first week of their attack of typhoid fever. The interval from onset ranged from 3 to 20 days. Each patient was given 3–4 tablets of 0·75 mgm. of dexamethasone (Decadron), together with 1–2 gm. of chloramphenicol (Farmicetina) daily. These doses were kept up for 2–3 days after the temperature had subsided and were then gradually reduced. The course of treatment lasted approximately 2 weeks and included 20–40 units of corticotrophin given in 2–4 doses; vitamins and liver extract were given and the diet was more or less unrestricted. Some 70% of the patients were apyretic within 24 hours, and all within 3 days except for 2 whose fever resisted 20 days of this treatment. There were no complications to speak of.

Corticosteroids can produce immediate, often dramatic, improvement in heavy infections, but they may at the same time favour serious complications by depressing the capacity of tissues to resist the infective agent.

J. Cauchi

RAVICH-BIRGER, E. D. & ANDREEVA, Z. M. **Methods of Detecting the Antigens of Dysentery Bacilli in the Excretions of Patients.** *J. Microbiol., Epidemiol. & Immunobiol.* London. 1960, v. 31, No. 6, 1032–7. [21 refs.] [Translated from Russian.]

This article opens with the statement that the antigens of dysentery organisms, destroyed by antibiotics and

chemotherapeutic agents, enter the blood stream and are excreted in the urine and saliva where the specific antigen or haptene can be recognized by appropriate techniques. The methods include precipitation tests on fresh serum, saliva and urine with *Shigella flexneri* and *Sh. sonnei* precipitating antisera; adsorption of the antigen in the urine with aluminium hydroxide and specific agglutination; preparations of haptenes from filtrates of serum, saliva and stools and subsequent precipitation tests or the adsorption of the haptenes on to rabbit red blood cells and subsequent agglutination tests. The adsorption techniques with either aluminium hydroxide or rabbit red cells proved to be the most suitable methods studied and were superior to the straightforward bacteriological culture method for the isolation of the infecting organism.

[This is not a critical article and it is often difficult to follow or to assess the importance of the work described.] *H. J. Bensted*

YOUNG, Viola M.; SOCHARD, Minnie R.; GILLEM, Harriete C.; ROSS, S. **Infectious Agents in Infant Diarrhea: I. A Hemagglutination-Inhibition Procedure for Detection of Bacterial Fractions in Infant Sera** [YOUNG, SOCHARD & GILLEM]. *Proc. Soc. Exper. Biol. & Med.* 1960, Dec., v. 105, No. 3, 635–8. [14 refs.] **II. Serological Reactions with *Escherichia coli* O1 through O25** [YOUNG, SOCHARD, GILLEM & ROSS]. *Ibid.*, 638–42. [22 refs.]

I. Sera of infants excreting enteropathogenic *Escherichia coli* may fail to show the presence of specific haemagglutinins because they contain trace amounts of unbound antigen or inhibitors which are related antigenically to the bacterial strains isolated from the patient's stools. The specificity of the inhibiting substance can be shown by using hyperimmune rabbit sera in a simple haemagglutination-inhibition test. For instance, *E. coli* 0.18 and *E. coli* 0.15 were isolated from the stools of a 7-month-old infant with diarrhoea. The acute-phase serum had an haemagglutinin titre of 128 for *E. coli* 0.18 and a 3-tube inhibition for 0.15. In another subject excreting 2 serotypes there were no haemagglutinin or inhibiting antibodies for one serotype but a 3-tube inhibition against the other serotype. Thus it would appear that the inhibiting substance in the serum of the patient is specifically related to the infecting organism in the bowel.

II. Although *E. coli* serotypes 0.26, 0.55, 0.86 and 0.111 are generally recognised as enteropathogenic, some of the so-called normal types of *E. coli* have, from time to time, been thought to possess pathogenic properties. The present paper is concerned with infants and young children with diarrhoea, from whom the generally recognised enteropathogenic serotypes have not been isolated, but only organisms classified serologically as *E. coli* with somatic antigens ranging from 0.1 to 0.25. Acute-phase and convalescent sera from these patients were examined for haemagglutinins and haemagglutination-inhibitors by quantitative tests. It was found that 12 out of 30 patients exhibited a rise in the haemagglutinin titre for the antigen of the organisms present in the bowel but that at some time during their illness two-thirds of the patients showed the presence, in their sera, of inhibitors which were antigenically related to the somatic antigens of the organisms isolated from their stools. The significance of these interesting results can only be assessed after a wider application of the methods. *H. J. Bensted*

DOTTI, F. & CASETTA, R. Osservazioni cliniche e terapeutiche sulla brucellosi in Provincia di Mantova. (Raccolta di 76 casi.) [**Clinical and Therapeutic Observations on Brucellosis in the Province of Mantua (76 Cases)**] *Igiene Moderna.* 1960, v. 53, Nos. 9/10, 469–86. [25 refs.] English summary (8 lines).

In a previous paper [this *Bulletin*, 1960, v. 35, 891] the authors have shown that brucellosis is especially prevalent in Mantua Province: they now report on a series of 76 cases seen during 1957–59. The patients were aged 15–73 years, and 67 were men. The authors treated 43 in their own hospital wards and saw the other 33 in consultation. Each patient had been followed up for at least 6 months after the signs and symptoms of the disease had gone.

One patient suffered from a chronic form which has resisted antibiotic and vaccine treatment for at least 14 months, 2 others had a one-sided orchitis and epididymitis, one patient had an acute hepatitis and there was a pneumonic localization in a fifth patient; the other 71 suffered no complications. The onset was acute in 51.

Details of the treatment which the authors gave their 43 patients are tabulated, with dosage and duration: 18 received aureomycin and streptomycin, 8 had aureomycin alone, 11 had chloramphenicol and 6 tetracycline. Corresponding details are tabulated for the other 33 patients.

No brucellae appear to have been isolated and the authors' comments on the species involved seem to lack the support of any bacteriological findings.

The disease seen in Mantua ran a benign course, mostly without complications, and proved generally amenable to simple antibiotic treatment. *J. Cauchi*

MARCHETTE, N. J., LUNDGREN, D. L., NICHOLES, P. S. & VEST, E. D. **Studies on Infectious Diseases in Wild Animals in Utah. I. Susceptibility of Wild Mammals to Experimental Tularemia.** *Zoonoses Res.* New York. 1961, Feb. 20, v. 1, No. 3, 49–73. [Numerous refs.]

This paper presents the results of quantitative experiments designed to assess the susceptibility of a number of different species of field rodents, rabbits, coyotes and other mammals which had been trapped in the wild state and exposed to deliberate infection with various strains of *Brucella tularensis*. The pathogenicity of different strains of *Br. tularensis* varies widely but generally the U.S. strains are more virulent than those found in the U.S.S.R. For instance, deer, mice and

wood rats were very susceptible to wild strains isolated locally from rabbits or their ticks, but quite resistant to one Russian strain and partially resistant to another. The paper contains very many interesting observations and should be read in the original form. The general conclusions are that tularaemia in the Great Salt Lake Desert Region of Utah is primarily a disease of jack rabbits and their ectoparasitic ticks (*Dermacentor parumapertus*) which can carry *Br. tularensis* throughout its life. Rodents may be involved but only incidentally, because the disease in these animals is generally so fatal that it is self-limiting and short-lived and because in this region the rodent populations are not sufficiently dense to support an epizootic even for a short period. The conclusions are based on the findings in the particular locality surveyed and cannot be assumed to have a general application.

H. J. Bensted

i. CLIFTON, B. S. **The Management of Tetanus.** *Med. J. Australia.* 1961, Apr. 29, v. 1, No. 17, 618–24. [13 refs.]

ii. MEDICAL J. AUSTRALIA. *Ibid.*, 630. **The Treatment of Severe Tetanus.**

i. This is a description of the therapeutic regime for tetanus practised at the Royal Prince Alfred Hospital, Sydney. This is based on 6 main principles, namely (1) sedation and relaxation, (2) tracheostomy, (3) artificial respiration, (4) intravenous therapy, (5) eradication of the disease and (6) prevention of infection. The regime is described in considerable detail and the article includes information on the technique of tracheostomy and the mechanics of artificial respirators. The article is long and detailed, contains nothing new, but emphasizes the need for meticulous care in the management of patients suffering from tetanus.

ii. An annotation calls attention to the necessity for treating all cases of tetanus in special centres capable of dealing with the most severe types. It is not yet agreed whether treatment should consist mainly of sedation or whether relaxant drugs combined with artificial respiration should be employed at an early stage. Chlorpromazine and paraldehyde or a barbiturate have been successfully used by several Australian workers in very severe cases, curarization being reserved for the few that fail to respond. PERLSTEIN *et al.* [this *Bulletin*, 1961, v. 36, 54] treated tetanus in heroin addicts in Chicago with intramuscular meprobamate and used chlorpromazine only when meprobamate failed; one advantage claimed was that even large intramuscular injections of meprobamate seemed to be painless. In most regimes tracheostomy is the rule and nutrition is maintained by intragastric tube feeding. Even in centres where curarization and artificial respiration are frequently used there is usually a preliminary treatment with sedatives, so that there is no radical difference of opinion between the two regimes. [It seems clear that even very severe cases of tetanus can be controlled without curarization; it is equally clear that curarization may save the otherwise hopeless case, but the treatment is highly specialized, requiring highly trained team work.] *A. B. Christie*

MADDOCKS, I. & DAWBORN, J. K. **Chlorpromazine given Orally in the Treatment of Severe Tetanus: a Case Report.** *Med. J. Australia.* 1961, Apr. 29, v. 1, No. 17, 625–6, 1 fig.

The authors treated a boy of 12 suffering from fairly severe tetanus with chlorpromazine and paraldehyde as sedatives. The chlorpromazine was given for the first 6 days intravenously, the paraldehyde by mouth. Venous thrombosis made further intravenous therapy impossible and the two drugs were then given by intragastric tube. The patient made a good recovery and the authors suggest that others might be encouraged to treat severe tetanus with chlorpromazine given by mouth and ancillary sedation, so reducing the call for aided respiration and intravenous therapy.

A. B. Christie

GERSTER, P. & MOESCHLIN, S. Klinische Behandlung des Tetanus mit Chlorpromazin. [**The Treatment of Tetanus with Chlorpromazine**] *Deut. med. Woch.* 1961, May 5, v. 86, No. 18, 890–97, 927–8, 2 figs. [66 refs.]

The main purpose of this paper is to record 7 cases of tetanus in 6 of which chlorpromazine was included in the scheme of treatment and was found to be of particular value and have the advantages over barbiturates that it has no significant effect on consciousness and respiration, relieves the feeling of fear, protects the patient from the pain and exhaustion of tetanic spasms and hence renders the management of patient easier for doctor and nurse.

The introduction contains much description and discussion based on numerous references and personal experience on the incidence of tetanus in different countries and on therapeutic principles. Sections of the paper are on antitoxin, active immunization, antibiotics, narcotics, curare preparations and dosage, combination of curare with chlorpromazine treatment, hibernation treatment and the use of cortisone preparations in puerperal tetanus.

There are clinical case reports of the 7 patients with particulars of the therapy employed. There were 2 deaths—a girl aged 6 years died on the 6th day of treatment from vasomotor collapse and a woman aged 80 who had hypertension and cardiac insufficiency on admission died suddenly on the third day.

A detailed recommended scheme of treatment is given. It includes débridement, active and passive immunization, administration of antibiotics, early tracheotomy and chlorpromazine in a dose of 25 or 50 mgm. intramuscularly at 2- to 8-hour intervals according to the severity of the case. In some but not in all instances sedatives may have to be given as well as chlorpromazine and in others treatment by curarization sometimes with artificial respiration may be indicated.

Chlorpromazine treatment is regarded as a very

great advance since in the majority of cases by its use alone the occurrence of severe spasms is prevented and only in exceptional cases is there need for curarization.
M. E. Delafield

LAURENCE, D. R. & WEBSTER, R. A. **Tachyphylaxis to the Anti-Tetanus Activity of some Phenothiazine Compounds.** *Brit. J. Pharmacol. & Chemotherapy.* 1961, June, v. 16, No. 3, 296–308, 9 figs. [23 refs.]

"Although chlorpromazine and acepromazine were the most potent suppressants of local tetanus induced in rabbits by intramuscular injection of the toxin of *Cl. tetani,* repeated injections lost their effect (tachyphylaxis) and sometimes even increased muscle activity, as did single large injections of either of the two drugs. As neither tachyphylaxis nor stimulation occurred in spinal animals, these effects might arise from an action in the brain-stem reticular formation on which chlorpromazine has been shown to have both inhibitory and excitatory effects. The possible cause of the tachyphylaxis is discussed. Evidence is advanced to support the view that tachyphylaxis can occur when chlorpromazine is used in the treatment of tetanus in man. Methotrimeprazine was more potent than chlorpromazine, but less prone to induce tachyphylaxis. These qualities rendered it more desirable for clinical use than the other two compounds."

BOCCIA, D. La leptospirosis en el ambiente rural. **[Leptospirosis in Rural Surroundings]** *Med. y Seguridad del Trabajo.* Madrid. 1960, Oct.–Dec., v. 8, No. 32, 5–17. [Numerous refs.]

LIBRACH, I. M. & SETH, R. K. **Human Listerial Meningitis.** *J. Clin. Path.* 1961, Mar., v. 14, No. 2, 193–5. [12 refs.]

"A case of Listerial meningitis is described in a man of 60 years. The aetiology of listeriosis is discussed."

VIRUS INFECTIONS

The order in this section is:—***General, Psittacosis-Lymphogranuloma group, Pox group, Respiratory group, Reovirus group, Enteric group, Arthropod-borne group, Others.***

MIDDELKAMP, J. N., HERWEG, J. C., THORNTON, Helen K., BROWN, J. H. & REED, C. A. **Viral Meningoencephalitis.** *J. Pediatrics.* St. Louis. 1961, Feb., v. 58, No. 2, 205–10. [20 refs.]

Satisfactory specimens for a virus diagnosis were obtained from 31 out of the 44 children admitted to the St. Louis Children's Hospital with a diagnosis of meningo-encephalitis between June and December 1958. A diagnosis was established in 26. 16 yielded type 1 poliovirus and all except 1 of these had spinal or bulbar paralysis. 11 of these patients were unvaccinated and 2 had had 3 doses of Salk vaccine. 2 patients had mumps meningo-encephalitis and 7 with meningitis were excreting ECHO 9 virus. 5 out of 6 examined had the virus in the cerebrospinal fluid. 1 patient suffered from Coxsackie B3 infection. This patient was admitted with weakness of both lower extremities but made a rapid and complete recovery.
A. J. Beale

SINNECKER, H. Zur Ätiologie postvaccinaler Encephalitiden. **[The Aetiology of Post-Vaccination Encephalitis]** *Zent. f. Bakt.* I. Abt. Orig. 1961, v. 181, No. 2, 150–54.

The author postulates that encephalitis following vaccination for smallpox may be due to the reactivation of an infection with tick-borne encephalitis virus, and produces circumstantial evidence in support of the hypothesis. The virus has been known to exist in Germany since 1959, and in a study of 14 cases of post-vaccination encephalitis it could be established that the patients all lived in close proximity to natural foci of the infection; in the case of a child who died of post-vaccination encephalitis, tick-borne encephalitis virus could be isolated from cows which supplied milk which had been consumed by the patient in the raw state; 7 patients had neutralizing antibody to tick-borne encephalitis virus in titres of 25–100. 6 other instances which suggest the activation of latent tick-borne encephalitis infection by poliomyelitis vaccination or by trauma are briefly described.
D. J. Bauer

PARNAS, J., SZMUNES, W. & ŁAZUGA, K. Ornitoza (choroba ptasia)—nowa choroba pracownicza w hodowli. **[Ornithosis, a New Occupational Disease in Breeding]** *Med. Pracy.* 1960, v. 11, No. 6, 411–20, 2 figs. [12 refs.] English summary (9 lines).

An investigation has been made of the incidence of ornithosis among workers in 6 poultry and egg packing plants in Poland. Ornithosis complement-fixing antibody was found in the sera of 37 of 694 persons in occupational contact with poultry in titres ranging from 8 to 64. No antibody was found in 29 hospital patients suspected of suffering from ornithosis, or in 581 ducks and hens sampled in 2 packing plants.
D. J. Bauer

MEIER, E. Die Pockenschutzimpfung in den Bundesländern und in Westberlin in den Jahren 1957 und 1958. **[Smallpox Vaccinations in Western Germany and West Berlin in 1957 and 1958]** *Zent. f. Bakt.* I. Abt. Orig. 1961, v. 181, No. 2, 155–74, 4 figs.

This is a very detailed description with a number of tables and figures of the extent to which smallpox vaccination has been carried out during 1957 and 1958 in each of the constituent states of Western Germany and in West Berlin. There is a very full analysis based

on official statistics of the numbers of children who are legally subject to vaccination (*Impfpflichtig*). These are grouped and subdivided into (1) those which have been vaccinated either (a) successfully (b) without success at the first or second and third attempts and (c) with an uncertain result and (2) those which have not been vaccinated either because of postponement, absence, withdrawal or other reasons.

The numbers are large. For example in 1957 there were about 1,132,000 registrations of children subject to vaccination in the different areas. Of this total, 634,000 children were successfully vaccinated in that year leaving 498,000 who were either unsuccessfully vaccinated or not vaccinated at all to be carried forward to the following year.

There is a very full description and discussion of this painstaking analysis. *M. E. Delafield*

ALIVISATOS, G. P., VIOLAKI-PARASKEVA, Meropi & KARANGHELI, Antigone, with the technical assistance of M. VARDALA. Die Virämie nach erfolglosen Vakzinationen mit verdünnter Lymphe. II. Mitteilung. [**Viraemia following Unsuccessful Vaccination with Attenuated Lymph**] *Ztschr. f. Immunitätsf. u. Exper. Therap.* 1960, Dec., v. 120, No. 5, 445–66, 9 figs.

The English summary appended to the paper is as follows:—

"1. Amnion cell cultures proved unsuitable for the demonstration of viraemia developing after successful vaccination. This viraemia mostly can be demonstrated qualitatively but not quantitatively on chicken embryos.

"2. Though the first vaccination with attenuated lymph mostly remains unsuccessful, persons thus ineffectively infected frequently develop a viraemia which certainly lasts for 14 days and perhaps even longer. Apparently the virus elements in this viraemia do not possess high infectivity, but may under certain conditions develop some.

"3. Revaccination of persons whose first vaccination was unsuccessful due to attenuation of the lymph nearly always is successful, provided an adequate vaccination dose is administered. Sometimes immunity can be demonstrated which does not last very long, but which is produced by the virus of the ineffective infection combined with viraemia.

"4. Sometimes a belated and accelerated reaction may occur which is caused by a partial immunity due to latent virus.

"5. A new nomenclature for the problems dealt with here, is suggested."

EHRENGUT, W. Über den Nachweis der vakzinalen Allergie mit formalininaktiviertem Vakzinevirus bei narbenlosen Wiederimpflingen. [**The Demonstration of Vaccinal Allergy with Formalin-Inactivated Vaccinia Virus in Persons with a Previously Unsuccessful "Take"**] *Deut. med. Woch.* 1961, Feb. 10, v. 86, No. 6, 264–6, 1 fig. on pl. [11 refs.]

The author has investigated the effect of vaccination with vaccinia virus inactivated with formalin in 25 persons aged 8–51 years who were due to be revaccinated and whose primary vaccination was considered to have been unsuccessful on account of the absence of a scar. An allergic reaction in the form of local erythema with slight infiltration appeared within 1–2 days in 15 persons, and began to regress after 3 days. A nodular reaction developed on revaccination with live vaccine lymph carried out 14 days later. The remaining 10 persons did not develop any reaction at the site of administration of the formalin-inactivated virus, but showed no greater reaction to revaccination 14 days later than the persons who had developed an allergic response. The results thus show that allergy to vaccinia virus is not necessarily associated with immunity. *D. J. Bauer*

APOSTOLOV, K., FLEWETT, T. H. & THOMPSON, K. S. **Death of an Infant in Hyperthermia after Vaccination.** *J. Clin. Path.* 1961, Mar., v. 14, No. 2, 196–7.

"Death following hyperpyrexia and coma of rapid onset nine days after vaccination of an infant is reported. Death appeared to be due to overwhelming vaccinial infection without encephalitis. Large amounts of virus was present in lung, spleen, bone marrow, and the vaccination site."

ROTEM, Y. & LEGUM, C. [**Varicella varioloformis**] *Harefuah.* Jerusalem. 1961, May 1, v. 60, No. 9, [in Hebrew 284–8, 6 figs. (30 refs.) English summary 288].

The English summary appended to the paper is as follows:—

"A fatal case of chickenpox in a 5 year old Yemenite girl is described. The child was admitted to hospital 10 days after onset of the illness as a case of suspected smallpox. The skin was very extensively involved and in fact showed many of the features of smallpox. The child's condition, critical on admission, deteriorated in spite of intensive treatment which included: broad spectrum antibiotics which were administered by the intravenous and intramuscular route, plasma and electrolyte solutions, human gamma-globulin given on consecutive days, and digitalis.

"Several severe complications including widespread subcutaneous emphysema, gastroenteritis, interstitial pneumonia and focal myocarditis were seen.

"The difficulty which occasionally occurs in differentiating chickenpox from smallpox is emphasized. Microscopic and microbiological examination of the contents of the skin vesicles and of the sputum are suggested as methods of establishing an early diagnosis.

"Although numerous authors have described the inclusion bodies of chickenpox as being eosinophilic, we found that many of them were basophilic. This is in accordance with the notion that the inclusion bodies found in viral diseases are viral colonies. Young inclusion bodies have a high DNA content and are basophilic

while older inclusion bodies have a low DNA and are eosinophilic."

DUNĂ, Florea & VOICULESCU, M. **Varicellous Herpes Zoster. With special reference to 3 Cases.** *Rumanian Med. Rev.* 1960, Oct.–Dec., v. 4, No. 4, 33–5.

CHANCELLOR, A. H. B. & MURPHY, A. M. **Herpes Simplex of Fingers.** *Med. J. Australia.* 1961, Apr. 8, v. 1, No. 14, 517–18, 1 fig.

"Vesicular lesions on the fingers of a child and the isolation from them of herpes simplex virus are described. Their similarity to bacterial lesions is noted." [See this *Bulletin*, 1960, v. 35, 261.]

RIGANTI, M. & BHAMARAPRAVATI, N. **Double Viral Infection in an Adult. Report of a Case of Disseminated Herpes Simplex Infection and Cytomegalic Inclusion Disease.** *Amer. J. Clin. Path.* 1961, May, v. 35, No. 5, 441–6, 5 figs. [16 refs.]

A case in a Thai woman aged 20.

UNITED STATES PUB. HEALTH SERVICE. NAT. INST. OF HEALTH. **International Conference on Asian Influenza, Bethesda, Maryland, Feb. 17–19, 1960.** *Amer. Rev. Respiratory Dis.* 1961, Feb., v. 83, No. 2, Pt. 2, pp. vii + 219, numerous figs. [Numerous refs.]

This number contains the text of papers and full transcripts of the discussion at a meeting held at the National Institutes of Health, under the auspices of U.S. Public Health Service. The conference was international in scope but the majority of the contributors were from the U.S.A. and a great deal of the information presented has been published elsewhere.

A. D. LANGMUIR (pp. 2–10) said that when the first Asian (A2) influenza strains were isolated virologists and epidemiologists agreed that they would produce a world-wide epidemic and would tend to spread in winter, and that this in fact occurred. Clinical illness affected mainly those between 10 and 20 years of age and the rate was apparently increased by crowding. After this first wave a second wave occurred in which adults and the elderly were affected and more deaths occurred. In discussion H. FUKUMI said that in Japan 20% of the population had antibody after the first wave and 45% after the second wave. A. M.-M. PAYNE (pp. 13–14) considered that a true second wave was seen in the U.S.S.R. and in Japan, but only an endemic phase in the U.S.A. and Britain. C. C. DAUER and R. E. SERFLING (pp. 15–26) gave final figures for influenza-associated mortality in the U.S.A.

W. S. JORDAN, Jr. (pp. 29–35) discussed the mechanism of the spread of influenza virus as revealed by the intensive study of families in Cleveland, Ohio. The introduction and attack rates were highest in children and lowest in fathers. Virus isolation and antibody rises were most frequent in children between 5 years old and the late 'teens. There was no clear evidence of intrafamilial spread, but the apparent secondary attack rate was 35%. The epidemic stopped when three-quarters of the school population had become infected. In discussion R. L. MCCLEAN (pp. 36–38) said there was a low incidence of influenza in a section of a tuberculosis hospital in which high level ultraviolet irradiation was installed.

Some influenza and influenza-like diseases of animals were reviewed by J. H. STEELE (pp. 41–46), M. SCHAEFFER and Rosalyn Q. ROBINSON (p. 47) and E. R. DOLL (pp. 48–50). C. H. STUART-HARRIS (pp. 54–61) said that the basic clinical picture of epidemic influenza has not changed over the 20 years during which laboratory confirmation of the diagnosis has been possible. Asian influenza may have produced rather more involvement of the central nervous system, croup and laryngotracheobronchitis than previous strains.

G. E. BURCH, J. J. WALSH and W. MOGABGAB (pp. 68–77) studied the cardiovascular system in 34 cases of influenza including 4 complicated cases. Rheoplethysmograms indicated vasoconstriction and reduced digital blood flow during the illness. Up to 75% of patients had minor ECG abnormalities, also detected on vectorcardiograms. Specimens were collected by bronchoscope from 9 patients at the height of the illness and showed degeneration of bronchial epithelium. D. P. EARLE (pp. 79–81) reported some rather similar findings.

J. F. P. HERS and J. MULDER (pp. 84–97) reviewed 148 virologically confirmed cases of Asian influenza. They recognized cytopathic changes in the alveolar epithelium, and using fluorescein-labelled antibody detected virus antigen in bronchial and alveolar cells.

T. FRANCIS, Jr. (pp. 98–104) expressed his views on most subjects discussed at the conference.

R. Q. ROBINSON (pp. 105–108) said the main differences between A2 and earlier strains were its antigens, its ability to agglutinate red cells of a wide range of species, and its very varied sensitivity to antibodies and non-specific inhibitors. C. H. ANDREWES (pp. 112–113) said that the O-D change was less prominent and that up to 1960 there had been little change in the antigenic composition of the strains isolated. A. F. RASMUSSEN (pp. 113–114) said that the haemagglutinin of Asian influenza is destroyed more readily by heat or ultraviolet irradiation than is the virus enzyme.

E. H. LENNETTE (pp. 116–119) and K. E. JENSEN (pp. 120–124) described the usual diagnostic tests for influenza. R. M. CHANOCK, K. M. JOHNSON, M. K. COOK, D. C. WONG and A. VARGOSKO (pp. 125–129) said that the haemadsorption test is positive in cells yielding myxoviruses and vaccinia but not ECHO virus, Reovirus or polyoma virus. The isolation rate of Asian influenza in tissue culture of monkey kidney cells was about 20%. Monkey kidney culture might contain a simian para-influenza virus, SV5, which was identical with the SA virus of SCHULTZ and HABEL [this *Bulletin*, 1959, v. 34, 832] and probably does not infect man.

C. Liu (pp. 130–132) described the diagnosis of influenza by staining the cells of nasal secretion with fluorescent antibody.

In discussion R. J. Huebner (pp. 135–136) pointed out that other acute respiratory disease was 10 to 20 times as common as influenza and that the amount of such illness in children under 17 equalled that in the rest of the population.

M. Schaeffer (pp. 139–141) said that only a few laboratories actually carried out important diagnostic work during the epidemic. Those set up in a hurry were not functioning till the epidemic was nearly over. C. H. Andrewes (pp. 142–143) suggested that laboratories be organized in 3 tiers with a "front line" laboratory at the bottom and an international reference laboratory at the top.

F. M. Davenport (pp. 146–150) suggested that vaccines might be improved by using purified haemagglutinin, not complete virus, as the antigen, and also using oil adjuvants.

J. E. Salk (pp. 153–156) advocated the use of emulsified antigens. "Cysts" at the inoculation site were due to toxic substance in the emulsifier, Arlacel A, which could be largely removed by purification. The vaccine was safer and more economical than saline vaccines. It could be used in children and there was no evidence that it was carcinogenic.

I. W. McLean, Jr. (pp. 157–159) described some of the difficulties in producing a vaccine in 4–6 months from the receipt of the strain and the order.

R. Murray (pp. 160–167) said that 42 million doses were distributed at the height of the epidemic [to be effective vaccine should have been administered *before* the height of the epidemic so it seems that this attempt at mass vaccination was only a little too late]. D. J. Davis (pp. 168–170) described the problem of allocation and distribution of vaccine but I. M. Rosenstock (pp. 171–174) indicated that only a small percentage of the public took any steps to get vaccinated without some sort of compulsion.

V. M. Zhdanov and V. D. Soloviev (pp. 178–187) said that 60 to 80% of cases of influenza yielded abnormal cells by "rhinocytoscopy". Live virus vaccine was administered in different areas and protection ratios varied from 1·3 to 3·6 with the lowest ratios in the largest groups. These vaccines were toxic to children.

The remaining authors gave their views on the value and function of the work of various health organizations in this and possible future outbreaks.

D. A. J. Tyrrell

Johnston, P. B. & Grayston, J. T. **Titration of Asian Influenza Neutralizing Antibody by Use of Hemadsorption Inhibition in Tissue Cultures.** *J. Infect. Dis.* 1961, Jan.–Feb., v. 108, No. 1, 19–24. [16 refs.]

A neutralization test was developed in which serum and virus were mixed and the presence of residual virus was detected by inoculating the mixture to monkey kidney cell cultures and testing 3 days later for the presence of virus by a haemadsorption test. It was found that virus grew well and reproducibly if the *p*H at the time of infection of cultures was 7·6 rather than 7·2 or 8·0. Non-specific inhibitors of haemagglutination did not seem to affect the test. Specific results were obtained in cross neutralization tests with some prototype myxoviruses and immune sera [though some rather unexpected cross reactions are also shown]. The method seemed to be a good way of detecting rises in antibody against Asian influenza virus in the sera of persons with the disease. 76 pairs of sera were tested with homologous virus. 49% showed a rise by complement-fixation, 61% by haemagglutination inhibition (HI) and 72% by neutralization. The persistence of antibody 1½ years after the attack was apparently demonstrated in "more than half" of "over 100" sera by this neutralization test but in only 5% by the HI test at the same dilution.

D. A. J. Tyrrell

Bamatter, F., Gautier, A., Jeanneret, O., Paccaud, M. F. & Wildi, E. Un cas d'encéphalite grippale avec isolement du virus A/Asia/57 dans le système nerveux central. [**A Case of Influenzal Encephalitis with Isolation of A/Asia/57 Virus from the Central Nervous System**] *Schweiz. med. Woch.* 1961, May 13, v. 91, No. 19, 567–71, 2 figs. [17 refs.]

The English summary appended to the paper is as follows:—

"This study deals with a fatal case of grippal encephalitis, where the same virus was isolated intra vitam from the cerebrospinal fluid and post mortem from the cerebral tissue and stool. Pathogenetic and diagnostic criteria of virus-conditioned encephalitic inflammations in general and of grippal encephalitis in particular are discussed. The cautious conclusion is that the isolation of a virus from the cerebrospinal fluid and from the brain does not suffice to prove the assumption that the virus attacked the central nervous system directly, as such swabs could have been taken in the course of viremia."

Byerliant, M. L. **Epidemiological Efficacy of Live Influenza Types A2, A, A-prime and B Vaccines.** *Problems of Virology.* London. 1960, v. 5, No. 1, 52–5. [Translated from Russian.]

Observations are reported on the effectiveness of monovalent A2 influenza vaccine and polyvalent A, A-prime and B vaccine during an outbreak of A2 influenza in Russia in October 1957. The epidemic occurred 2 weeks after immunization of 1,400 persons with the monovalent vaccine (control unvaccinated group of 850 persons) and at the start of immunization of 1,150 persons [according to the text; a table gives the figure 1,500] with the polyvalent vaccine (control group 900). The communities were uniform in age, living conditions and type of occupation. Immunization with monovalent vaccine caused a 2-fold decrease in the incidence of disease while the polyvalent material had little effect. However, immunization with the

polyvalent vaccine 3 months before an outbreak primarily due to A-prime virus in February 1956 reduced the incidence of disease among inoculated persons by half. [Placebo preparations were not given to the control groups.] *D. Taylor-Robinson*

GUTEKUNST, R. R. & HEGGIE, A. D. **Viremia and Viruria in Adenovirus Infections. Detection in Patients with Rubella or Rubelliform Illness.** *New England J. of Med.* 1961, Feb. 23, v. 264, No. 8, 374–8. [17 refs.]

122 U.S. naval recruits with rubelliform disease were studied over 18 months; 96 subjects of the same population mainly with minor injuries and without respiratory complaints were selected at random as controls. Garglings, rectal swabs, throat swabs and paired sera were collected (only last 2 specimens from controls). All specimens except the second serum sample were inoculated into primary monkey kidney, Salk monkey heart, HeLa cells and Chang human liver tissue cultures, in most cases immediately after collection. Adenoviruses (types 4 and 7) were isolated from the throat swabs of 22·1% of men with a rash and from 23·9% of the controls. 55% of those from whom a virus was isolated (both subjects with a rash and controls) showed a 4-fold complement-fixing antibody rise. Virus was isolated from 10 acute-phase sera of subjects with a rash but not from 140 control persons, and virus was also isolated from 11 of 32 urine specimens (concentrated 10-fold) from persons with a rash. Urine specimens were not collected from control subjects. On the basis of the demonstration of the viraemia the authors suggest that adenoviruses occasionally produce a rubelliform eruption.

D. Taylor-Robinson

VAN DER PLOEG, G. C. J., STRENGERS, L. & VAN DER VEEN, J. Onderzoek over het etiologische verband tussen adenovirus en "viruspneumonie" bij kinderen. [**A Study of the Aetiological Relationship between Adenovirus and Virus Pneumonia in Children**] *Nederl. Tijdschr. v. Geneesk.* 1961, May 6, v. 105, No. 18, 861–7, 3 figs. [14 refs.]

The English summary appended to the paper is as follows:—

"Sixteen cases of acute infection of the lower respiratory passages and/or lungs in children admitted from May, 1958 to May, 1959, were studied for the possible presence of adenovirus as a causative agent. A significant rise in complement fixing antibody against adenovirus was seen in 10 cases. Adenoviruses were recovered in 9 out of 10 serologically positive cases. Type 7 virus was isolated from 6 patients, type 4 from 2 patients and type 3 from 1 patient. Complement fixation tests for influenza A and B, para-influenza 1, 2 and 3, psittacosis and Q fever, as well as tests for cold agglutinins were negative in all cases. The clinical, radiographic and haematological data are reported. No significant differences in clinical features were found between adenovirus-positive patients and patients whose virological and serological findings were negative. All viral pneumonias observed were sporadic cases from the general population. Most of the children were under 3 years of age. The high incidence of adenovirus 'pneumonias' may have resulted from an increased spread of type 7 virus among the Dutch population in 1958 and 1959."

SOBĚSLAVSKÝ, O. Konglutinační komplement absorpční test v diagnostice adenovirových nákaz. [**Conglutinating Complement Absorption Test in the Diagnosis of Adenovirus Infections**] *Československ. Epidemiol., Mikrobiol., Imunol.* Prague. 1961, v. 10, No. 3, 206–11, 2 graphs. [13 refs.]

The English summary appended to the paper is as follows:—

"Into the serological diagnosis of adenovirus infections the conglutinating complement absorption test [KKAT] was introduced. In the submitted paper the method is described in detail and the results obtained are compared with those of the complement fixation reaction.

"A total of 161 sera were examined and compared. From an analysis of the results obtained by both tests it appears that the KKAT, as compared with the complement fixation reaction makes it possible to estimate antibodies in most instances in four times higher titres. Eight times higher titres were found only less frequently. The finding of so-called non-specific titres (1:10 and less) were much less frequent than in the complement fixation reaction. The disadvantage of the test, as compared with the latter, is that a large number of anticomplementary sera are detected.

"The complement absorption test can be used with advantage in those instances where in the investigated sera complement fixing antibodies are present in low or not easily detectable titres."

KINGSTON, J. R., CHANOCK, R. M., MUFSON, M. A., HELLMAN, L. P., JAMES, W. D., FOX, H. H., MANKO, M. A. & BOYERS, J. **Eaton Agent Pneumonia.** *J. Amer. Med. Ass.* 1961, Apr. 15, v. 176, No. 2, 118–23, 2 figs. [13 refs.]

Of 290 patients suffering from bacteriologically negative pneumonia 109 developed a serological response for Eaton agent only, 24 were positive for Eaton agent and another respiratory virus, 35 were positive for other viruses and 122 were negative for the 11 agents included in the test. A double blind therapeutic trial with demethylchlortetracyclin showed that patients suffering from Eaton agent pneumonia responded well: duration of fever, rales, cough, malaise and fatigue were all reduced. The treatment had no apparent effect on patients suffering from other known respiratory viruses, but in the group suffering from pneumonia of undiagnosed cause there was a good response though less marked than in the Eaton agent group. Cold agglutinins developed in 47% of Eaton-positive pneumonia but only in 7% of Eaton-negative cases. *A. B. Christie*

DELVILLE, J. P. & PATTYN, S. R., with the technical collaboration of J. PEEL. Étude longitudinale des virus entériques chez des enfants d'une communauté congolaise à Elisabethville. **[Longitudinal Study of Enteric Viruses in Children of a Congolese Community in Elizabethville]** *Ann. Soc. Belge de Méd. Trop.* 1960, Dec. 31, v. 40, No. 6, 879–92, 3 graphs. [19 refs.]

This interesting study concerns the excretion of viruses in the stools of children examined at fortnightly or monthly intervals for the first 14 months of life. In all, 24 Congolese children were studied and 17 were bled at the end for poliovirus antibody titrations. Out of 408 stool samples 159 yielded viruses. 130 strains were isolated in tissue culture and 49 in suckling mice. They were identified as follows: 9 poliovirus, 4 Coxsackie B, 94 Coxsackie A, 30 ECHO, 12 adenovirus and 30 unidentified. Only 1 child was triple negative for poliovirus at 14 months and 9 were triple positive. Virus isolations were relatively rare under 6 months but thereafter around 50% of the samples contained a virus. The rate of isolation depended upon age of children rather than on family size.

A. J. Beale

SANCHIS-BAYARRI, V. Étude de l'immunisation spontanée contre la poliomyélite à Valence (Espagne). **[Studies on Natural Immunization against Poliomyelitis in Valencia, Spain]** *Ann. Inst. Pasteur.* 1961, Apr., v. 100, No. 4, 531–8, 3 figs.

A serological survey in Valencia, Spain, for poliovirus antibodies is described. 203 sera from children under 10 were tested. By 10 years 84% had antibodies to all 3 types and 50% had them by 5 years. However, at 2 years over 70% of the children had no antibodies to any type of poliovirus. *A. J. Beale*

MILANOVIC, M. V. & MIRKOVIC, R. R. **Studies on Poliomyelitis in Serbia. I. Survey of Neutralizing Antibodies to Polio Virus in Serbia in 1954, and Isolation of Virus 1952–1954.** *Acta Med. Iugoslavica.* 1960, v. 14, No. 4, 446–65, 5 figs.

A serological survey for poliovirus antibodies was made in Serbia. Sera were collected in 1954 from 453 patients seen in clinics with diseases other than poliomyelitis. Statistical sampling methods were not employed. The results showed that antibodies to all 3 types of poliovirus were common in Serbia. Antibodies were least prevalent to type 1. Only 20% of the children under 4 years had antibodies to type 1 whereas in the same age group 80% had type 2 antibodies and 50% type 3 antibodies. Even in adults only 50–60% had type 1 antibodies. Urban populations had a higher rate of acquisition of polio antibodies than rural populations. All 3 types of poliovirus were isolated from patients. Type 1 accounted for 55%, type 3 for 40% and type 2 for 5%. The incidence of type 2 antibodies was lower in patients with type 1 or 3 virus paralysis than in the general population, suggesting that type 2 antibodies may protect against the other 2 types of poliovirus. *A. J. Beale*

TAUBE, E. **The Presence of Circulating Antibodies to Polio Virus in a Small Series of Northern Rhodesia Africans.** *Central African J. of Med.* 1960, Oct., v. 6, No. 10, 421–2.

The author reports on antibody surveys in Africans, mostly children; 88 specimens were from the urban area of Lusaka, and 106 from the rural Mankoya district of Barotseland. In each area one-half or more of the children had been infected by the age of 4 years, and almost all by the age of 5–9 years. All 3 types of virus antibodies were prominent.

The author has not seen acute poliomyelitis in an African child who has outgrown the toddler stage, but recalls the common observation of tragic cases in Europeans, especially new immigrants. He comments [as others have done] that all young immigrants from Europe should be immunized with Salk vaccine before starting work in Northern Rhodesia.

Charles Wilcocks

YANG, Czau-Siung, LAI, Juey-Shin, SHIAO, Liu-Ching & KAO, Ming-I. **Age Distribution of Poliovirus neutralizing Antibodies in Taipei Area.** *J. Formosan Med. Ass.* 1960, June 28, v. 59, No. 6, 423–9, 6 figs. [14 refs.]

A survey of poliovirus neutralizing antibodies in Taipei area in 1958 and 1959 is reported. 234 assorted sera were examined (127 healthy children, 40 patients not suffering from poliomyelitis, 31 adults and 36 cord bloods). They revealed that poliovirus infection is very common. Adult sera and cord bloods had similar titres, usually less than 1/64 to all 3 types. The majority had antibodies to at least one type by 3 years of age but even in adults only about 50% had antibodies to all 3 types. Poliomyelitis in Taiwan occurs predominantly in children under 2 years. All 3 types of poliovirus have been isolated but in 1958 and 1959 type 1 was mainly responsible. *A. J. Beale*

OSTFELD, A. M. **Sustained Hypertension after Poliomyelitis.** *Arch. Intern. Med.* 1961, Apr., v. 107, No. 4, 551–7. [22 refs.]

32 of 159 adolescents and young adults with chronic poliomyelitis had a higher than normal blood pressure years after their acute illness. This hypertension was not related to hypertension in the acute stage or to urinary infection or stones. The authors feel that the cause lies in the diminution in number of arterioles and other minute vessels in atrophied muscle. When central venous pressure rises, a baroreceptor system in the right atrium or great thoracic veins leads to increase in cardiac output. Such increase in normal subjects does not lead to increased blood pressure as peripheral resistance drops to accommodate it. In chronic poliomyelitis

the diminution in peripheral arterioles makes such accommodation impossible and hypertension results.

A. B. Christie

HENNESSEN, W., MAULER, R., RESTLE, H. & KÖRNER, L. Untersuchungen an einem Vierfach-Impfstoff mit Poliomyelitisanteil. **[The Antigenic Potency of Quadruple Vaccine containing Killed Polio Virus]** *Deut. med. Woch.* 1961, Apr. 28, v. 86, No. 17, 861–5, 883, 5 figs. [19 refs.]

The English summary appended to the paper is as follows:—

"Quadruple vaccine (against polio, diphtheria, pertussis and tetanus) was tested by single injection in children not previously immunized for the mutual influence of the various antigens on antibody response, for possible side-effects, and for its antigenicity. Given suitable conditions, there was no demonstrable antigen incompatibility, no general or localized reaction, and satisfactory antibody response even after the initial injection. Contrary findings by some other investigators are discussed: they are explained by the techniques employed which did not conform with the conditions laid down for the testing of polio vaccine."

MELNICK, J. L., BENYESH-MELNICK, Matilda, PEÑA, R. & YOW, Martha. **Effectiveness of Salk Vaccine. Analysis of Virologically Confirmed Cases of Paralytic and Nonparalytic Poliomyelitis.** *J. Amer. Med. Ass.* 1961, Apr. 1, v. 175, No. 13, 1159–62. [10 refs.]

Advances in virology have shown that many cases clinically diagnosed as non-paralytic poliomyelitis are not due to poliovirus and that a smaller number of paralytic cases cannot be confirmed by laboratory study. It is evident, therefore, that the assessment of polio-vaccine effectiveness requires laboratory confirmation of the cases to be fully valid, as has been shown by LENNETTE and his colleagues [this *Bulletin*, 1960, v. 35, 479; 1961, v. 36, 679]. In this study 126 subjects with this diagnosis of paralytic poliomyelitis and 125 with abacterial meningitis occurring in the Houston area in 1958–59 were examined. 102 of the paralysed patients yielded a virus, 100 of which were polioviruses. The history of killed poliovaccination of these 100 patients was: 0 doses, 87; 1 or 2 doses, 10; and 3 or more doses, 3. The non-paralytic cases yielded 53 viruses, 43% polioviruses and 57% non-polio enteroviruses (including 10 as yet untypable new ECHO viruses). Recovery of poliovirus was rare in triply vaccinated children, but vaccination status had no influence on the other viral causes of meningitis.

A. J. Beale

WEIHL, C., CORNFELD, D., RILEY, H. D., HUANG, Nancy & CRAMBLETT, H. **Purified Poliomyelitis Vaccine —Clinical Appraisal.** *J. Amer. Med. Ass.* 1961, May 6, v. 176, No. 5, 409–12, 2 figs. [13 refs.]

Poliomyelitis continues to be a serious problem in the United States despite the proved efficacy of killed polio-vaccine given in at least 3 doses. This is mainly because of the failure of immunization programmes to cover a sufficiently high proportion of the population but also because of the deficiencies of vaccine potency. This paper records results achieved with Purivax (Merck Sharp and Dohme Research Laboratories) which is a purified, concentrated poliovaccine standardized for amounts of poliovirus antigen by spectroscopy. The efficacy of this vaccine in two 0·5 ml. doses 1 month apart was compared with ordinary Salk vaccine (of better than average potency). Earlier batches of purified vaccine suffered from losses due to virus adsorption on to the glass. This was avoided by the addition of Tween 80 to the medium used to resuspend the vaccine. Vaccine containing 3·2 μgm. of virus antigen gave 98% conversion for all 3 types of virus compared with 81, 100 and 97% for the crude poliovaccine. The geometric mean titres were not significantly different.

These results are considerably better than those reported by KOKKO and MURRAY [this *Bulletin*, 1960, v. 35, 793] for "run of the mill" U.S. killed polio-vaccine which gave conversion rates of 50, 94 and 46% to types 1, 2 and 3, respectively. The superiority of the purified vaccine is more clearly illustrated if sero-conversion is taken at the 1/16 instead of the 1/4 level. The advantages of a pure, standardized product are stressed. Results following a booster dose and studies of the durability of the antibodies are promised.

A. J. Beale

RITZEL, G., SCHÄR, M., PLOTKIN, S. A. & KOPROWSKI, H. Massenimpfung von Schulkindern mit Lebendimpf-stoff gegen Poliomyelitis **[Mass Inoculation of Schoolchildren With Live Polio Vaccine]** *Schweiz. med. Woch.* 1961, June 3, v. 91, No. 22, 656–8.

The English summary appended to the paper is as follows:—

"17,600 school children who had previously been immunized by 3 injections of Salk-vaccine were fed live attenuated poliovirus type I (Chat-Strain of Koprowski). No complications were observed. A high degree of efficacy was verified by serological tests. In $\frac{2}{3}$ of the children who—in spite of 3 injections of Salk-vaccine—had little or no antibody against type I poliovirus, titer levels higher than 1:1,000 were observed. No child was without antibodies after feeding live attenuated virus.

"There were no clinical or epidemiological signs pointing to an eventual increase in the virulence of the attenuated virus by human passage. It may therefore be assumed that wide spread use of oral poliomyelitis vaccine is a safe and effective method for the control of poliomyelitis."

POLIOMYELITIS RES. FOUNDATION, Johannesburg. **Memorandum on Oral Poliomyelitis Vaccine.** *South African Med. J.* 1961, Mar. 25, v. 35, No. 12, 253–6. [Also published in *Med. Proc.* Johannesburg. 1961, Mar. 25, v. 7, No. 6, 111–16.]

This memorandum describes the oral attenuated polio-vaccine made by the Poliomyelitis Research Foundation

in Johannesburg and recommends methods for its use. The vaccine is made from Sabin's strains. Pathogenic bacteria and viruses are excluded, as are non-pathogenic simian viruses. Also, an appropriate [but unspecified] chemical treatment is used as an extra safeguard. The dose recommended is at least 10^5 TCD50. The vaccine is sent out concentrated so that 1 ml. contains 10^7 TCD50. The method of administration favoured is from an automatic syringe which sprays the vaccine to the back of the throat, but drops in syrup or on sweets are also acceptable methods. The importance of storing the vaccine at $-20°C$. and the exercise of aseptic precautions (since it contains no preservative) in dispensing and diluting it are stressed. The recommended schedule is monovalent vaccine in the order type 1, 3 and 2 with intervals of 2 months between doses and finally a trivalent mixture. 3 doses of a trivalent mixture may be equally satisfactory.

Alimentary immunity develops quickly in about 4 days and antibodies usually develop in 1 week. A table shows the results that have been obtained based on serological conversion. 1 feeding of trivalent vaccine fills about 70% of the gaps in immunity and 3 doses nearly 100%.

The vaccine is clearly safe. Over 90 million doses have been given without causing a single proved case of paralysis. There are considered to be no serious reactions or contra-indications. On general principles, febrile bed-ridden patients are not vaccinated, nor are those with diarrhoea. Surgery is not recommended within 2 weeks of a dose, nor vaccination within 1 week of an operation. It is recommended that other vaccines should not be given within 14 days of oral poliovaccine lest reactions to these should discredit poliovaccination. It is also recommended that no carbonated, alcoholic or other flavoured drinks or medicines should be taken within 2 hours of vaccination. The only way of assessing the effect of vaccination is to titrate neutralizing antibodies.

[This is an informative memorandum about attenuated poliovaccine for potential users. There is no reference to the literature.] *A. J. Beale*

COOPER, E. D. & ROBERTSON, W. I. **Problems resulting from the Use of Live Attenuated Poliomyelitis Virus Type I in a Mass Campaign in a Large Urban Area.** *South African Med. J.* 1961, Mar. 18, v. 35, No. 11, 232–5.

As the use of attenuated poliovaccine becomes accepted Medical Officers of Health will face the problems of administering it. They will find this account by the Medical Officer of Health for the City of Cape Town, who is the senior author, very helpful and informative. It is a factual account of a programme of oral poliovaccination with vaccine made from Sabin's strains by Dr. J. H. GEAR in Johannesburg. The details of the campaign are given. The need for advance planning and publicity is stressed if the desired population (pre-school and school children) are to be reached in the shortest possible time. Infants under 4 months were not vaccinated, nor were adults over 40 years unless they asked specially. Infants had vaccine in syrup and the vaccine was dropped on to absorbent sweets for older children. The methods proved easy to administer. There were no serious reactions to the vaccine.

[This paper should be read in the original by any medical officer considering an attenuated poliovaccine programme.] *A. J. Beale*

PAGANO, J. S., PLOTKIN, S. A. & KOPROWSKI, H. **Variations in the Responses of Infants to Living Attenuated Polivirus Vaccines.** *New England J. of Med.* 1961, Jan. 26, v. 264, No. 4, 155–63, 2 figs. [31 refs.]

The response of 96 infants to attenuated poliovaccine was investigated. The strains used were CHAT type 1, P-712 type 2 and W-Fox type 3. The response to oral vaccination, whether assessed by virus excretion or antibody response, varied with age. Excretion occurred in over 90% of the infants under 1 week old as it did in those over 10 weeks old. In between these ages excretion was less frequent, occurring in 73%. Antibody response was poor in the youngest infants and improved with increasing age. Under 1 week of age only 53% responded (despite the high virus excretion level) and over 10 weeks 90% responded. Age was more important than maternal antibody levels in determining virus excretion. Antibody responses were probably masked by high levels of maternal antibody. In assessing antibody responses allowance was made for the half life of maternal antibodies, estimated at 18 days. There were, however, wide individual fluctuations in the rate of decline in antibodies. Intestinal infection was related to dose, being uniformly successful with over $10^{6\cdot1}$ TCD50, about 80% successful in the range $10^{4\cdot1\text{-}6\cdot0}$ and less successful below this level.

Viruses were usually given in the order 1, 3, 2 and an interval of at least 4 weeks between doses was considered desirable so that interference between strains could be avoided. Virus given in combinations of either 3 or 2 types together was unsatisfactory. With doses under 10^7 TCD50 pharyngeal excretion was rare. Children who failed to make an antibody response despite virus multiplication did so usually (5 out of 6) after refeeding. All who had no evidence of infection at the first attempt were successfully infected in refeeding. 4 out of 8 successfully infected the first time excreted virus and 3 out of the 8 made an immune response on refeeding, but the duration of excretion was much reduced. *A. J. Beale*

GAISFORD, W., FELDMAN, G. V. & PERKINS, F. T. **The Response of Infants to Poliomyelitis Immunization after Neonatal Immunization with Triple Antigen.** *J. Pediatrics.* St. Louis. 1961, Apr., v. 58, 493–8, 3 figs.

There are many possible schedules for immunization against poliomyelitis, diphtheria, tetanus and pertussis in infancy. The response of young infants to 2 doses of poliovaccine when there are high levels of maternal antibodies is not good. On the other hand, the use of triple antigen adsorbed on to aluminium phosphate in

children without poliomyelitis antibodies may carry the risk of provocation paralysis as pointed out by a Medical Research Council [this *Bulletin*, 1957, v. 32, 233] investigation. The authors have therefore immunized women in pregnancy with 3 doses of killed poliovaccine and, thereafter, the infant with triple antigen at 1, 5 and 9 weeks. The children were given killed poliovaccine at 9, 10 and 13 months. Out of 31 mothers only 1 was triple negative; in all, 7 lacked type 1, 5 type 2 and 5 type 3 antibodies. After 3 doses all had high levels of antibody to types 2 and 3 and all but 1 had antibodies to type 1. The levels in mothers' and cord sera blood were closely similar.

The responses to pertussis, diphtheria and tetanus were good, most children having no detectable maternal antibody. 3 failed to respond to pertussis and these had titres of 1/16 in the cord blood. 6 failed to respond to diphtheria and again all these had maternally transmitted antitoxin. All infants responded to the tetanus component. 17 children were given poliovaccine and, after 3 doses, the responses were also excellent. Most of the maternal antibody titres had fallen to 1/16 or less. Only 1 each for types 1 and 2 and 3 for type 3 had levels of 1/64. The response to type 2 was best. Only 1 infant (titre 1/16) had a titre of less than 1/8192 and only 2 infants (1/128 and 1/16) had titres under 1/2048 for type 3. The type 1 responses, although not so good, were also impressive, only 3 (1, 1/8 and 2, 1/32) being less than 1/128.

The authors feel that this schedule, although immunologically satisfactory, is not suitable for general use. They state that there are indications that a quadruple antigen with more potent poliovaccine can overcome the inhibitory effect of maternal antibodies.

A. J. Beale

SWANN, N. H. **Epidemic Pleurodynia, Orchitis, and Myocarditis in an Adult due to Coxsackie Virus, Group B, Type 4.** *Ann. Intern. Med.* 1961, May, v. 54, No. 5, 1008–13, 4 figs.

"A case of Bornholm disease complicated by orchitis and myocarditis in the adult is presented. The etiologic agent was found to be Coxsackie virus, group B, type 4. This is believed to be the first reported occurrence of myocarditis in the adult due to group B, type 4 of the Coxsackie viruses."

GILL, E. & GORBY, E. W. Myokarditis und Perikarditis infolge Coxsackie-Virusinfektion. [**Coxsackie Myocarditis and Pericarditis**] *Deut. med. Woch.* 1961, June 23, v. 86, No. 25, 1234–6. [30 refs.]

HAMMON, W. McD., YOHN, D. S., PAVIA, Rose A. & SATHER, Gladys E. **ECHO Virus Type 13. II. Epidemiologic Aspects and Clinical Associations.** *Amer. J. Trop. Med. & Hyg.* 1961, Jan., v. 10, No. 1, 62–6. [18 refs.]

The first ECHO 13 prototype was isolated in the Philippines during a longitudinal study of poliovirus infection in United States Air Force families. It was found to be a mixture of ECHO 1 and 13, the new prototype being defined by HAMMON *et al.* [this *Bulletin* 1959, v. 34, 837]. The virus was originally isolated from 10 healthy children and has since been isolated by ROSEN *et al.* [*ibid.*, 1958, v. 33, 1097] from the Washington Junior Village community and in Pittsburgh by Cheever and Abraham (personal communication to the authors) from children with diarrhoea and fever. 2 patients who had serological evidence of ECHO 13 infection are described. 1 had mild paralytic "poliomyelitis" and the other aseptic meningitis. 2 monkeys (out of 16 monkeys inoculated by various routes) inoculated intracerebrally and intraspinally developed chronic meningoencephalitis. *A. J. Beale*

SEDDON, J. H. **An Epidemiological Survey of Infectious Hepatitis in a Country Town.** *New Zealand Med. J.* 1961, Feb., v. 60, No. 342, 55–60, 3 figs. [17 refs.]

In 1958 an epidemic of infectious hepatitis occurred in Mangakino, New Zealand, a township with a population of about 5,000 persons and a surrounding country area with a population of 1,300. One-third of these populations are Maori. To review this outbreak all the notifications of the disease between April 1956 and mid-1960 were considered. The number of these was 70 of which 48 were in 1958. Minor outbreaks were in spring 1957, summer 1959 and autumn 1960.

The notifications do not give a complete picture of the incidence since some icteric and most non-icteric cases are excluded.

There is a good account of the investigations which were made to attempt to discover the sources of infection. The evidence so obtained led to the opinion that the outbreak in 1957 was probably milk-borne and that those in 1958, 1959 and 1960 were probably water-borne.

In the series of 70 patients there were 33 females and 37 males. There were only 13 notifications of Maori patients and the average age of these was 5 years with a range of 3 months to 16 years. The average age of the 57 European patients on the other hand was 20 years with a range of 6 weeks to 45 years. There was no definite seasonal pattern but the highest incidence was in late summer. The attack rate was significantly higher in the town than among the population of the surrounding country. There is a good discussion of the findings of the survey. *M. E. Delafield*

VOICULESCU, M., ZAMFIRESCU, I., CĂRUNTU, Veronica, ISTODOR, N., VALERIU, A., RĂDULESCU, M., DEDIU, S., BOCÎRNEA, C., DUMINICĂ, A., PĂUN, L., RĂDVAN-GEORGESCU, A. & VLAD, R. **Treatment and Prophylaxis of Hepatic Coma in the Course of Epidemic Hepatitis.** *Rumanian Med. Rev.* 1960, Oct.-Dec., v. 4, No. 4, 29–32.

The authors treated cases of hepatic coma and precoma by the following routine: no protein by mouth, repeated enemata and the use of tetracycline and sometimes neomycin to cut down the activity of ammonia-producing intestinal organisms; 20 gm. sodium glutamate

solution every 24 hours, glucose solution to produce adequate calorie intake, the control of hydro-electrolytic and acid base balance, oxygen, cortisone in large doses (200–700 mgm. daily) and high doses of vitamins. 12 of 15 pre-coma patients and 3 of 18 coma patients survived. The authors felt that the most definite results were achieved by corticosteroids when applied to pre-coma patients. If all patients are carefully supervised and the full treatment is applied at the first sign that the case is becoming severe the authors hope that coma may be prevented. *A. B. Christie*

Olson, T. A., Kennedy, R. C., Rueger, M. E., Price, R. D. & Schlottman, L. L. **Evaluation of Activity of Viral Encephalitides in Minnesota through Measurement of Pigeon Antibody Response.** *Amer. J. Trop. Med. & Hyg.* 1961, Mar., v. 10, No. 2, 266–70, 3 figs.

At several sites 60 pigeons were exposed in wire mesh cages. They were bled before exposure and at approximately monthly intervals thereafter and tested for neutralizing antibody to Western encephalitis virus (RML strain No. 85). In an area where an epidemic occurred in 1941, 68% of the pigeons developed antibody in 1958 between June and October, and 24% in 1959. In the transition zone between a glacial lake and an upland area about 120 miles farther south the conversion rates were similar. In the central region of the State the conversion rates were 34 and 32% respectively. 2 pigeons at this station also developed St. Louis encephalitis antibody. In a mosquito control district in 1958 there were no conversions. In an area where epidemic equine encephalitis had occurred in the late 1930s only 2% converted. An attempt is being made to correlate these findings with mosquito activity.

C. E. Gordon Smith

Sărăteanu, D., Drăgănescu, N. & Lisievici-Oprescu, Elena. Cercetări asupra prezenței anticorpilor antiencefalitici la lucrătorii forestieri. [**Studies on the Presence of Anti-Encephalitis Antibodies in Forest Workers**] *Microbiol., Parazitol., Epidemiol.* Bucharest. 1961, Mar.–Apr., v. 6, No. 2, 121–5. [27 refs.]

The English summary appended to the paper is as follows:—

"Investigations with regard to the presence of anti-encephalitis antibodies in forest workers were carried out in four different regions, by means of the complement fixation test. Positive results were obtained in 21 of the 43 sera tested, the proportion of positive tests being much higher in the region where the encephalitis virus had been previously isolated from a clinical case. The presence of positive complement fixation reactions in healthy persons, without encephalitis in their past history, but living or working in forest regions, lends support to the assumption that there are a great number of subclinical forms of encephalitis."

Pogodina, V. V. **Epidemiology and Prevention of Alimentary Infections of Tick-Borne Encephalitis.** *J. Hyg., Epidemiol., Microbiol. & Immunol.* Prague. 1961, v. 5, No. 1, 75–9. [12 refs.]

Alimentary infections with tick-borne encephalitis virus have been found in all parts of the Soviet Union—both in foci of *Ixodes ricinus* and of *I. persulcatus.* However, the proportion of alimentary infections is very low in the Far East, forms 3·5–23% in the Urals, and reaches 61–85% in the West. Alimentary infections cause milder disease than tick infections but the severity and incidence of central nervous system disease increase from west to east.

In a study of 114 cases in the Urals and Western Siberia these alimentary infections were found to occur in families and other groups and 33% were in patients aged under 7 years. The incubation period was 1–14 days. [The former period seems too short.] 33% of patients had biphasic illness. Of 38 groups of patients, in only 9 groups were all those exposed to unboiled milk affected. Many of those who did not fall ill developed antibody. 74% of the goats and 80% of the cattle in these areas had antibody. Antibody was found most often in persons who drank unboiled goats' milk and in only a few who drank cows' milk.

Control is discussed, based on insecticide treatment of pastures and milk-producing animals and on vaccination of such animals. 2 doses of killed vaccine concentrated with aluminium hydroxide or 1 dose of an attenuated live vaccine have produced good antibody responses in goats, with few or no symptoms.

C. E. Gordon Smith

Levkovich, J. N. **A Survey of the Dynamics of the Virus of Tick-Borne Encephalitis on the Basis of Serological Investigations.** *J. Hyg., Epidemiol., Microbiol. & Immunol.* Prague. 1961, v. 5, No. 1, 80–84. [11 refs.]

In a study in 1937–8 of sera from 586 persons in a focus of tick-borne encephalitis in the Far East 51% of those in close contact with nature were found to have antibody, compared with 45% in those living in settlements. In those who had been in an area under 6 months no antibody was found but after 1–2, 3–4 and 5–6 years in the area 27, 36 and 47% respectively had antibody. Of old settlers in rural Western Siberia in 1956 80–90% had antibody—in the same area there was a high incidence of the disease in new inhabitants and the virus was isolated from 20–40% of the ticks. In patients with the disease 34% developed antibody 15–30 days after onset. In persons bitten by ticks in previous years 3–15-fold increases of antibody occurred in 2·5–4 weeks.

In 1959 at Picktack in the West Siberian Taiga, collections were made of wild mammals and birds and of ticks. The ticks were predominantly *Ixodes persulcatus* but *I. trianguliceps* and gamasids were also present. 77% of the wood- and field-mice and 43% of the Siberian hares and *Eutamicus asiaticus* were found to have antibody. None was found in house-mice. 6 of 14 birds (mainly fieldfares) had antibody but none of 9 nestlings.

Large-scale collections of animals have recently been made and tissue extracts are to be tested for antibody because of the difficulty of obtaining sufficient blood. Experiments suggest that antibody titres in such extracts are similar to those of the blood.

C. E. Gordon Smith

ROSICKÝ, B., TOVORNIK, D., BRELIH, S., DANIEL, M., NOSEK, J. & MACICKA, O. Zur Bionomie der Zecke *Ixodes ricinus* L. in Naturherd der Zeckenenzephalitis in den Steiner Alpen (Kamniške Alpe-Slovenija). [**Bionomics of *Ixodes ricinus* in a Natural Focus of Tick Encephalitis in the Kamnik Mountain Region**] *Českoslov. Parasit.* Prague. 1961, v. 8, 305–23, 7 figs. [14 refs.]

TRENCSÉNI, T. & KELETI, B. Die hämorrhagische Nephroso-Nephritis in Ungarn und in Europa. [**Haemorrhagic Nephroso-Nephritis in Hungary and Europe**] *Acta Med.* Budapest. 1960, v. 16, No. 3, 303–11, 2 figs. [28 refs.]

In 1953 the authors observed for the first time in Hungary cases of a disease which resembled the haemorrhagic nephrosa-nephritis hitherto recognized only in the Far East. Up to the present time 112 cases have been recorded in Hungary, occurring as 10 sporadic cases and in small epidemics of up to 31 cases. Their distribution is shown on a map, and a complete list is presented in a table. A well-developed renal syndrome occurred in 72 cases, and in the remainder the disease took an abortive course; the spleen was palpable in 43 cases; 1 was fatal. The occurrence of recognized cases of the disease since 1948 in the Soviet Union, Czechoslovakia, Bulgaria, Yugoslavia, Sweden, Finland and Norway is discussed in conclusion. *D. J. Bauer*

ANDERSON, S. G., PRICE, A. V. G. & WILLIAMS, M. C., with the technical assistance of Margaret MCELROY & NANADAI-KOIA. **Antibody to Murray Valley Encephalitis and Louping-Ill Viruses in Australia and Papua-New Guinea.** *Med. J. Australia.* 1961, Mar. 25, v. 1, No. 12, 444–7, 1 fig. [28 refs.]

16 sentinel chickens were exposed in April 1957 at each of 5 places within 50 miles of Port Moresby, New Guinea. Of 67 surviving in August 1957, none had Murray Valley antibody. In August 1958, 0 of 6 (from 2 sites in one area), 1 of 6, 5 of 12 and 10 of 10 at the 5 places had developed antibody with titres between 50 and 500. 5 similar groups of chickens were exposed in the Northern Territory in June 1958. In November 1958, eggs from them were tested for antibody in the yolk to Murray Valley virus and none was found. This was repeated in July 1959 but only 1 positive was found. In November 1958, 76 domestic chickens at Mildura in the Murray Valley were bled—all had been alive since August 1957, a period during which no clinical cases of Murray Valley encephalitis had been reported. No antibody was found.

210 human sera from various places in the eastern half of Australia and from New Guinea were tested for antibody to louping ill virus; 4 positive sera with low titres were found from Queensland or New South Wales. All of them also had antibody to Murray Valley virus and the authors think that both antibodies may be heterologous, representing antibody to another group B virus.

The history of work on the epidemiology of Murray Valley virus is reviewed. *C. E. Gordon Smith*

KARELITZ, S. & EISENBERG, M. **Measles Encephalitis. Evaluation of Treatment with Adrenocorticotropin and Adrenal Corticosteroids.** *Pediatrics.* Springfield, Ill. 1961, May, v. 27, No. 5, Pt. 1, 811–18. [15 refs.]

This is a study of 42 patients suffering from measles encephalitis treated between 1952 and 1958. At the time of admission 23 patients were in coma, 15 were lethargic and 30 were in convulsions. Yet all recovered. All had intensive nursing and medical care and 20 had in addition corticosteroids, adrenocorticotrophins or both. Steroid therapy made no difference to the recovery rate or to the incidence of sequelae and the authors question the value of these drugs in the management of measles encephalitis. [The survival of 42 consecutive cases of measles encephalitis is remarkable.]

A. B. Christie

GIBBS, F. A., GIBBS, Erna L. & ROSENTHAL, I. M. **Electroencephalographic Study of Children immunized against Measles with Live Attenuated Virus Vaccine.** *New England J. of Med.* 1961, Apr. 20, v. 264, No. 16, 800–801. [12 refs.]

"Electroencephalographic tracings were done on 40 children, ten days after immunization with attenuated measles virus and were compared to records taken immediately before immunization. In contrast to results obtained in a previous study of natural measles, no electroencephalographic abnormality was found that could be attributed to infection with the attenuated measles virus."

LIPPI, M., CORSO, P. & FRUGONI, G. Contributo sieroimmunologico alla conoscenza delle principali virosi. Ricerca nei soggetti sani degli anticorpi devianti il complemento verso il virus della coriomeningite linfocitaria. [**Study of Complement-Fixing Antibodies against Lymphocytic Choriomeningitis Virus in Healthy Persons**] *Arch. Ital. Sci. Med. Trop. e Parassit.* 1961, Mar., v. 42, No. 3, 109–24. [53 refs.]

The English summary appended to the paper is as follows:—

"Serum antibodies fixing the complement towards the antigen of lymphocytic choriomeningitis have been studied in a sample of healthy Roman population consisting of 380 individuals; 12·8% of the examined sera were positive."

Di Nola, F., Martano, M. & Giuliani, G. Su 37 casi di mononucleosi infettiva. **[Observations on 37 Cases of Infective Mononucleosis]** *Giorn. di Malattie Infettive e Parassit.* 1961, Mar., v. 13, No. 3, 144–6. [13 refs.]

Molteni, H. D., Guarinos, H. C., Petrillo, C. O. & Jaschek, F. Estudio clínico estadístico sobre 338 pacientes afectados por la fiebre hemorrágica epidémica del noroeste de la Provincia de Buenos Aires. **[Clinico-Statistical Study of 338 Patients suffering from Epidemic Haemorrhagic Fever in the North-East of Buenos Aires Province]** *Semana Méd.* 1961, Apr. 24, v. 118, No. 21, 838–55, 878, 11 graphs. [33 refs.]

Acute epidemic haemorrhagic fever, or "Mal de los Rastrojos" is extensively present in the north-east of the province of Buenos Aires. A severe outbreak which occurred in 1958 was followed by intensive investigations and this paper reports certain epidemiological and clinical findings in 338 patients admitted to the infectious disease wards of the regional hospital at Junín between March and September 1959.

The disease has certain important epidemiological features: the lowest incidence is in the autumn and winter; males are affected 5 times as frequently as females; by far the greatest number of cases are in people aged 15–44 years, and, finally, agricultural workers make up over 80% of cases. Starting in March the incidence rises to a high peak in mid-May, falls to a lower plateau in June and there are subsidiary peaks in April and July. The general case-fatality rate was 5%, though out of 85 patients admitted in May, 10 died. The prognosis was greatly affected for the better by early diagnosis and admission to hospital.

Slight, moderate, and severe types of illness can be distinguished clinically, beginning with an initial stage often resembling influenza, progressing through a well-marked florid stage to convalescence. An important point is that, according to the tables, of the 212 cases of initially slight type of illness, one-third became moderately severe, or severe in the florid stage. All 17 deaths occurred in the severe grade and the prognosis was especially grave in patients presenting with predominantly nervous or cardiac symptoms, especially the former.

The main features of the disease were arterial hypotension, bradycardia, high temperature in the florid stage (even over 40·5°C.), haemoconcentration, and leucopenia, most marked in the gravest cases. Thrombocytopenia was found in up to 88% of 246 patients; it gradually returned to normal during the recovery stage but this was much slower than the patient's clinical recovery. The erythrocyte sedimentation rate was abnormally low. No case of either renal or hepatic disease was found, which is in marked contrast with previous findings. The haemorrhagic syndrome was rare in the initial stage, and only 109 out of 321 patients showed any evidence of haemorrhages, all of which were mucosal. In the fatal cases death was due in almost every instance to haemorrhage or encephalitis.

The authors do not give their views as to causation.

[For earlier work see this *Bulletin*, 1960, v. 35, 278.] *W. K. Dunscombe*

Bacteriology and Immunity

The order in this section is:—**General; Bacteriostatic and Bactericidal Substances; Bacteria; Rickettsiae; Bacteriophages; Viruses; Immunity.**

Abstracts of papers relating to the bacteriology of plague, cholera, yaws, leprosy and certain other tropical bacterial diseases; of the rickettsial fevers; and of yellow fever, dengue, rabies and certain other tropical virus infections, are published in the TROPICAL DISEASES BULLETIN. *Their titles and page references are cited below in the appropriate sub-divisions of this section.*

GENERAL

McLeod, Joyce A. & McLeod, J. W. **The Technique and Interpretation of Tests for Leucocidin with special reference to the Value of Ethylene Diamine Tetra-Acetic Acid (EDTA).** *Brit. J. Exper. Path.* 1961, Apr., v. 42, No. 2, 171–8, 2 coloured figs. on pl. [13 refs.]

Polymorphonuclear leucocytes which survive exposure to a potential leucocidin can be recognized by the oscillation of their granules [this *Bulletin*, 1959, v. 34, 564] and by their ability to reduce methylene blue to its colourless form. Thus they remain apparently unstained when exposed to dilute concentrations of the dye in hypotonic saline.

Difficulties due to delayed and irregular coagulation following the harvesting of the leucocytes are now obviated by using the sodium salt of ethylene diamine tetra-acetic acid (EDTA) as anticoagulant in place of

heparin and substituting dextran for the ox fibrinogen which assisted separation of the cells. The leucocytes so obtained are resuspended in plasma and are then exposed to dilutions of the leucocidin in Hanks solution containing 0·1% EDTA. Where incubation of 20 hours or more is required (and where the toxic action is not ion-dependent and controlled by the chelating agent) this solution is superior to 0·85% saline or to Hanks solution alone. The cells are subsequently exposed to 1:2000 methylene blue in 0·3% saline and examined within 10 minutes.

Neutral red had been used previously as the indicator dye. Methylene blue however is shown to be much less toxic and therefore less likely to cause fallacious appearances of leucocidal action by the substance under test.

The significance of cells showing anomalous staining or granular oscillation after exposure is discussed.

J. M. Stark

McLeod, Joyce A. & McLeod, J. W. **The Absence of Leucotoxic Activity in Highly Purified Diphtheria and Tetanus Toxins (as bearing on the Virulence of the Bacteria Concerned).** *Brit. J. Exper. Path.* 1961, Apr., v. 42, No. 2, 179–86. [46 refs.]

Ørskov *et al.* (*Acta Path. et Microb. Scandinavica*, 1944, v. 21, 181) have shown that in lesions due to highly virulent strains of *Corynebacterium diphtheriae* there is a lack of leucocyte response which can be reversed by the antitoxin. Using their newly reported technique [see above], however, the authors find that the purified diphtheria toxin itself is not leucotoxic. These observations together suggest that a separate leucotoxic substance is also produced by virulent strains.

Tetanus toxin does not have any leucotoxic activity.

J. M. Stark

Noble, W. C. **The Size Distribution of Airborne Particles carrying *Clostridium welchii*.** *J. Path. & Bact.* 1961, Apr., v. 81, No. 2, 523–6.

Air samples were collected with the size-grading sampler [Lidwell, this *Bulletin*, 1959, v. 34, 921] and with a slit sampler, on to a medium modified from that of Lowbury and Lilly [*ibid.*, 1956, v. 31, 676] for the selective isolation of *Clostridium welchii*. In surgical wards the number of airborne particles carrying *Cl. welchii* varied between 0·03 and 0·74 per cu. ft. 78% of the airborne particles had an equivalent diameter of more than 4·2 μ; the proportion of large particles was lower in wet weather than in dry. The size distribution of particles carrying *Cl. welchii* resembled that for *Staph. aureus* and differed from the distribution for *Bacillus*-carrying particles, which are commonly less than 4·2 μ in diameter.

R. E. O. Williams

Meyers, C. E.; James, H. A.; Zippin, C. **The Recovery of Aerosolized Bacteria from Humans. I. Effects of Varying Exposure, Sampling Times, and Subject Variability** [Meyers, James & Zippin] *Arch. Environment. Health.* Chicago. 1961, Apr., v. 2, No. 4, 384–90. [24 refs.] **II. Estimation of Number of Samples necessary for Specified Assurance of Detecting Exposure to an Indicator Organism** [James, Zippin & Meyers]. *Ibid.*, 391–6, 3 figs.

I. Aerosols of *Chromobacterium prodigiosum* (*Serratia marcescens*), consisting largely of particles 1–3 μ in diameter, were inhaled by human subjects. The oropharynx was then sampled by swilling and gargling with saline [see Ostrom *et al.*, this *Bulletin*, 1959, v. 34, 147]. The proportion of subjects yielding the bacteria in the oropharyngeal samples varied with the dose inhaled, from about 20% with doses of 1–49 to 63–78% for doses of 500 or more. Even with doses of over 5,000, the proportion of recoveries declined from 66% to 13% in 1 hour. Different subjects varied substantially. It is pointed out that, even with such small particle sizes, a substantial number of organisms are retained in the upper respiratory tract.

II. The records of the work reported in the previous paper are analysed to show the likelihood of detecting the recent inhalation of a given dose of micro-organisms by sampling the oropharynx, or alternatively the number of individuals to be examined for there to be a given probability of detecting one harbouring the bacteria. The results are presented in tables and graphs.

R. E. O. Williams

Sussman, M., Barnes, R. & Lenihan, J. M. A. **The Design and Testing of an Ultraviolet Irradiated Box for Hand Dressings.** *Lancet.* 1961, May 27, 1143–4, 4 figs.

A simple Perspex box mounted on a table and fitted with 2 15-watt ultraviolet lamps, is arranged so that the patient can insert a hand from one side, and the nurse can work from the other side, putting her (gloved) hands through a narrow aperture. There is an arrangement for discarding the dressings into a bag from within this box. Bacteriological tests showed that an aerosol of staphylococci was quickly killed by the irradiation, but no clinical tests are reported.

R. E. O. Williams

Work, Elizabeth. **The Mucopeptides of Bacterial Cell Walls. A Review.** *J. General Microbiol.* 1961, June, v. 25, No. 2, 167–89, 2 figs. [Numerous refs.]

Roman, H. **Genetics of Some Microorganisms.** *Amer. J. Human Genetics.* 1961, Mar., v. 13, No. 1, Pt. 2, 107–12. [18 refs.]

BACTERIOSTATIC AND BACTERICIDAL SUBSTANCES; DISINFECTION

The order in this section is:—**General; Antibiotics; other Therapeutic Substances; Disinfection.**

WILLIAMSON, G. M., MORRISON, J. K. & STEVENS, K. J. **A New Synthetic Penicillin PA-248.** *Lancet.* 1961, Apr. 22, 847–50.

This paper is from the Department of Bacteriology, School of Medicine, Leeds, and the Clinical Research Department, Chas. Pfizer Ltd. PA-248 is a α-phenoxypropyl penicillin, and in these studies it was compared with phenethicillin (α-phenoxyethyl penicillin) and penicillins V and G. In a triple cross-over study in 12 normal subjects the blood content was assayed after a single oral 250 mgm. dose of each of these penicillins except G. PA-248 gave the highest levels, distinctly higher than phenethicillin and much higher than V: the means in μgm./ml. after 1, 2, and 4 hours were PA-248, 6·22, 1·74 and 0·53; phenethicillin, 5·26, 1·46 and 0·46; V, 1·63, 0·32 and 0·07 (the differences between phenethicillin and V are wider than any previously reported, and the scatter in individual results is very wide, *e.g.*, from 11·4 to 0·43 for PA-248 at 1 hour).

The results are also expressed as antibacterial activity in units of penicillin G, and these place the 3 penicillins in the same order of activity with smaller differences [presumably the antibacterial activity referred to here is against *Sarcina lutea*, the only assay organism mentioned, but this is not stated in the table of results]. Minimum inhibitory concentrations (MIC) of the 4 penicillins for several strains of 7 species of bacteria were determined by a tube dilution method. The activity of PA-248 corresponded closely to that of phenethicillin, as might be expected from its similar structure: minor differences were a somewhat greater activity against resistant staphylococci, not much affected by inoculum size, which also suggests relative resistance to penicillinase, and a slightly lesser degree of activity against sensitive staphylococci and gonococci. There are no significant differences between them in results with pneumococci, meningococci, *Haemophilus influenzae* and *Streptococcus pyogenes*, but as the authors point out, and has been shown before [this *Bulletin*, 1961, v. 36, 284], penicillin G is more active than any of the oral penicillins against Gram-negative species.

[The results given for *Strep. pyogenes* are inexplicable: the MIC of all 4 penicillins for 2 strains of this organism are given as 2 or 4 μgm./ml.: this is 200-fold in error, at least for a Group A strain and penicillin G.]

L. P. Garrod

NAGLEY, M. **Clinical Use of a New Synthetic Penicillin: PA-248.** *Lancet.* 1961, Apr. 22, 851.

PA-248 was administered in a dose of 250 mgm. 4 times a day to 9 patients with staphylococcal lung infections, described as consolidation in 6 and as cavitation, pneumonitis and infiltration in 1 each. 5 of the patients were infected with penicillin-resistant staphylococci, the remainder being sensitive. An unstated number of patients with similar infections all due to penicillin-sensitive staphylococci were treated with the same doses of penicillin V. Staphylococci were eliminated from the sputum of all patients in both groups, and the responses of the 2 groups as judged by other criteria were equal. It is emphasized that in the PA-248 group the response in penicillin-resistant infections was the same as in the sensitive. The paper is very short, giving no details beyond the bare facts stated here.

L. P. Garrod

GILLISSEN, G. & REITZ, H. Abbauprodukte des Penicillins und deren biologische Bedeutung für das Resistenz-problem. I. Darstellung und Abbaukinetik von Penillsäure. **[Decomposition Products of Penicillin and their Biological Significance for the Problem of Resistance. I. Isolation and Decomposition Kinetics of Penillic acid]** *Zent. f. Bakt.* I. Abt. Orig. 1961, v. 181, No. 1, 34–50, 10 figs. II. Die Wirkung von Penillsäure und Phenylessigsäure. **[II. The Action of Penillic acid and Phenylacetic Acid]** *Ibid.*, 51–62, 8 figs.

This work derives from that of MARKOV and SAEV [this *Bulletin*, 1957, v. 32, 497], who found that penicillic or penicilloic acid could replace thiamine as a growth factor for penicillin-resistant but not for sensitive strains of staphylococci: other degradation products of penicillin, penicillamine and phenylacetic acid, had no such effect. The first of these papers describes the preparation of penillic acid, and an elaborate study of its physical properties, methods for its extraction, assay etc. The second reports observations on the effect of penillic acid and phenylacetic acid on penicillin activity against staphylococci, as judged by determinations of minimium inhibitory concentration, generation time and oxygen consumption. Penillic acid was found to be without any effect. Phenylacetic acid, on the other hand, reduced the activity of penicillin against sensitive strains of staphylococci and enhanced the activity against resistant strains. The degree of these effects varied with concentration. Apart from any bearing they may have on the work of Markov and Saev, it seems that these findings are presented as a warning against possible errors due to the existence of degradation products in penicillin.

L. P. Garrod

SUBHIYAH, B. W. **Severe Immediate Reactions to Penicillin. Report of Five Cases including One Fatality.** *J. Facul. of Med., Baghdad.* 1961, Jan., v. 3 (n.s.), No. 1, 30–36. [22 refs.]

This is said to be the first report of such reactions to penicillin in Iraq. In the 5 cases described they varied

in severity, but all were immediate and characterized by vasomotor collapse. 3 of the patients are recorded as having had penicillin before, and 1 of them, a doctor, had had a reaction from it before on 2 previous occasions. The most apparently severe case recovered: this was a woman who rapidly became unconscious, pulseless, cyanosed and incontinent, and after partial recovery passed so much blood per rectum that she had to be transfused: the intestinal bleeding in this condition is said to be previously unrecorded. The fatality was in a "28 year-old sturdy athletic young chemist employed as a drug-store propogandist" who asked a doctor to give him an injection of penicillin for sinusitis: after partial recovery he died shortly after admission to hospital despite appropriate treatment. The author discusses treatment and prevention, advocating [as innumerable other authors have done] that penicillin should be given only for rational indications and not to everyone with fever, that enquiry should be made before giving it about previous reactions, and that adrenaline and other remedies should always be instantly available. *L. P. Garrod*

FAIRBROTHER, R. W. & TAYLOR, G. **Sodium Methicillin in Routine Therapy.** *Lancet.* 1961, Mar. 4, 473–6. [15 refs.]

These authors have verified observations previously made by others, *viz.* that *Staphylococcus aureus*, regardless of whether it is sensitive or resistant to penicillin G, is consistently inhibited by the same concentration (in their tests 4 or 8 μgm./ml) of methicillin, and that this effect is almost unaffected by inoculum size. These observations, made on 150 strains of which only 20 were sensitive to penicillin G, include tests with erythromycin, by which the great majority were inhibited in a concentration of 0·25 or 0·5 μgm./ml. The bactericidal action of penicillin was also demonstrated. In habituation experiments, 2 penicillinase-forming strains became 16- and 32–fold more resistant to methicillin in 10 transfers in medium containing this antibiotic, and this change was accompanied by a considerable loss of resistance to penicillin G. A strain originally sensitive to penicillin G underwent an 8–fold increase in resistance to methicillin when subjected to the same procedure. The authors refer to these results as showing that "staphylococci readily develop resistance in vitro" to methicillin. "It is recommended that methicillin should be reserved for severe infections caused by *Staph. aureus* resistant to the usual antibiotics".

[For previous references, see this *Bulletin*, 1961, v. 36, 173, 174, 175]. *L. P. Garrod*

ORENTREICH, N., HARBER, L. C. & TROMOVITCH, T. A. **Photosensitivity and Photo-Onycholysis due to Demethylchlortetracycline.** *Arch. Dermat.* 1961, May, v. 83, No. 5, 730–37, 11 figs. (10 coloured on pl.) [13 refs.]

"Exaggerated sunburn-like reactions after demethylchlortetracycline ingestion were noted in 27 of 108 ambulatory dermatologic patients. 7 showed photo onycholysis.

"Data presented suggest that the photosensitivity wa of the phototoxic type with an action spectrum in the wavelength range between 2,750 A. and 3,100 A., and that it was readily reversible.

"Characteristics of the DMCT phototoxicity are lowered erythema threshold, an increased intensity o erythema response, and a persistence of erythema afte ultra-violet light exposure.

"No evidence of hepatic, renal, or hematologi changes was noted in any of the patients taking DMCT."

[See this *Bulletin*, 1960, v. 35, 689 *bis*.]

SOCIÉTÉ FRANÇAISE DE MICROBIOL. (Séance du 3 Nov 1960.) Réunion d'un groupe d'étude sur les anti biotiques du groupe colistine-polymyxine. **[Meeting of a Study Group on the Antibiotics of the Colistin-Polymixin Group]** [WELSCH, M., President]. *Ann. Inst. Pasteur.* 1961, Apr., v. 100 No. 4, Suppl. 88 pp., 12 figs. [Numerous refs.]

This supplement consists of 10 papers presented a the meeting referred to in the title. These deal almos exclusively with colistin from various points of view and none has anything positive to say about the nature of the relationship of this recently discovered antibiotic to polymyxin, which was discovered years earlier, and clearly differs from colistin little, if indeed at all.

R. BOURSE and J. J. MONNIER (*Introduction to the study of bacterial sensitivity to colistin. Analysis of results obtained by 4 laboratories*, pp. 7–13). 4 laboratories were given the task of determining the minimum inhibitory concentration (MIC) of colistin for 7 strains of *Escherichia coli* and 1 each of 8 other organisms by defined methods. The results were satisfyingly concordant, but they showed that the antibiotic is consistently more active in one of the media used than in the other and that the sulphate is more active than the methane sulphonate.

A. L. COURTIEU, J. J. MONNIER, P. de LAJUDIE and Francoise N. GUILLERMET. (*Antibacterial spectrum of colistin for 1200 strains*, pp. 14–31). These authors determined the MIC of colistin sulphate by a plate dilution method for 1,229 strains of a great variety of bacteria. The results are given in numerous tables and provide valuable detailed information, much of which is new. Gram-positive organisms in general, both cocci and bacilli, were resistant, as were fungi and BCG. *E. coli* (many serotypes tested), was usually highly sensitive, but 12/406 strains were resistant to 100 μgm./ml. Results with *Salmonella*, *Shigella*, *Pseudomonas* and various coliform species were similar, but *Proteus* were all resistant. Among other Gram-negative rods, *Haemophilus*, *Bordetella* and *Pasteurella* were sensitive, and *Brucella* and *Malleomyces* resistant. A few strains of Gram-negative anaerobes (*Fusiformis* etc.) were sensitive as were "various" *Neisseria*, but gonococci and meningococci were unpromisingly resistant. Many less familiar and less important organisms than those mentioned were tested.

J. C. PATTE and Y. A. CHABBERT. (*Modes of antibacterial action of colistin*, pp. 32–43). The mode of

action of colistin was studied by exposing a strain of *E. coli* and a *Klebsiella* to different concentrations and following the changes turbidimetrically and by viable counts. Colistin is rapidly bactericidal, but a "rebound" effect is seen after exposure to lower concentrations, *i.e.*, re-growth after an initial fall in the viable count. Bactericidal effect is conditioned by inoculum size and medium: it is accompanied by a decrease in turbidity, but this is said to be less than that caused by polymyxin.

Y. A. CHABBERT and J. C. PATTE. (*Type and characteristics of bacterial resistance to colistin*, pp. 44–52). These authors discuss resistance to colistin in sensitive species, adducing evidence that large populations can contain a few resistant cells and that one-step mutation to resistance can occur readily, as can back-mutation to normal sensitivity. The emergence of resistant organisms can be a cause of therapeutic failures, *e.g.*, in urinary tract infections.

Y. A. CHABBERT. (*Curves of bacteriostatic action of combinations of colistin with tetracyclines and kanamycin*, pp. 53–58). This is a study of the nature of the combined action of colistin and 2 other antibiotics on 38 strains of *E. coli* or *Klebsiella* and 6 of *Pseudomonas* by 2 methods. Colistin and tetracycline frequently acted synergically: a similar but more obscure effect was seen less often with colistin+kanamycin.

J. J. MONNIER and R. BOURSE. (*Direct and cross resistance of Escherichia coli to colistin in vitro*, pp. 59–66). Attempts were made to render 13 strains of *E. coli* resistant to colistin by the usual habituation procedures: 8 were unchanged and 5 increased in resistance 16- or 32-fold. This change was accompanied by a closely corresponding increase in resistance to polymyxin. Comparison of the MIC of colistin and polymyxin for 111 strains of enteropathogenic *E. coli* also showed close correspondence: these included 12 strains not inhibited by 100 μgm./ml. of either antibiotic.

A. L. COURTIEU, N. BOULEZ, Suzanne CHASSIGNOL and J. M. BOTTA. (*Bacteriological study of an epidemic of specific E. coli enteritis in a community of infants and children. Study of sensitivity of colistin*, pp. 67–70). This concerns an epidemic of gastro-enteritis caused by *E. coli* O,127: B, 8 which occurred in an infants' nursery in Lyons. The infection was treated with colistin, polymyxin or sulphaguanidine, all given by the oral route. Towards the end of the epidemic, colistin-resistant organisms were found in the faeces of 4 infants who had recovered.

P. de LAJUDIE. (*Application of diffusion methods to colistin*, pp. 71–76). This is a study of the use of diffusion methods for determining sensitivity to colistin. The diameter of the inhibition zones was much affected by the composition of the medium, notably its organic salt content. The cup is more dependable than the disc method, but a dilution method is preferable to either.

S. LECLERCQ. (*Nephelometric assay of colistin*, pp. 77–83). This paper describes a nephelometric method for the assay of colistin, with *Klebsiella pneumoniae* and a medium containing yeast extract to produce rapid growth. The rate of growth of this organism is very sensitive to small differences in colistin concentration: it also varies much with the size of the inoculum. If coliston methane sulphonate is being assayed, this must also be used for the standard. Solutions of this salt increase in activity during the first 24 hours after their preparation, a phenomenon so far unexplained.

A. DODIN, E. R. BRYGOO and S. RAJENISON. (*Action of colistin and polymyxin on Pasteurella pestis in vitro. Action of colistin in experimental plague in the mouse*, pp. 84–88). These authors from Madagascar studied the action of colistin on *Pasteurella pestis in vitro* and *in vivo*. Determinations of the MIC (with 10-fold differences) showed 14/22 strains to be inhibited by 0·2 μgm./ml., the remainder by 2 or 20. Some tests were also done with polymyxin; in a Table 4 strains are shown as inhibited by 0·02 μgm./ml. (including 2 for which the MIC colistin is 100 times greater) and no results are stated for the other strains, but the text gives other results including a statement that 1 strain was "totally resistant" to polymyxin. Colistin was shown to be rapidly bactericidal. Mice inoculated with a large multiple of a lethal dose (of a not fully sensitive strain, according to the Table) were treated with colistin by subcutaneous injection, and from 8/20 to 19/20 survived according to dosage and time of administration.

L. P. Garrod

JAGO, M. & HEATLEY, N. G. **Some Biological Properties of Cephalosporin C and A Derivative.** *Brit. J. Pharmacol. & Chemotherapy.* 1961, Apr., v. 16, No. 2, 170–79, 1 fig. [13 refs.]

Cephalosporin C is one of several antibiotics produced by the same fungus (which include cephalosporin N, or synnematin B), and was at one time looked upon as therapeutically promising because it is bactericidal, resistant to penicillinase and strikingly non-toxic [FLOREY, this *Bulletin*, 1956, v. 31, 441]. The yield is small, and difficulties of production evidently explain why so little has been heard of it for several years.

This paper describes a comprehensive study of both cephalosporin C and a pyridine derivative of it known as "cephalosporin C_A (pyridine)". Minimum inhibitory concentrations of these two, cephalosporin N and penicillin G were determined for 25 species of bacteria. Highly susceptible organisms include the pyogenic cocci, *Neisseria* spp. and some Gram-positive bacilli: the pyridine derivative is more active against most of these, but less so than cephalosporin C itself against *Vibrio cholerae*, which is also highly susceptible. Both forms of cephalosporin C were almost as active against penicillinase-forming staphylococci as against penicillin-sensitive, and no destruction of either antibiotic by penicillinase could be detected. Their activity is unaffected by the addition of 50% serum to the medium. Some resistance to both could be induced in staphylococci by the usual procedures. *In vivo* tests included demonstration of a very low intravenous toxicity in mice. When either form was given by this or the subcutaneous route to mice it attained high but rapidly falling levels in the blood and was wholly excreted in the urine within 6 hours. After oral administration less than 5% appeared in the urine and it was shown that much remained in the bowel although more was unaccounted for. In a therapeutic test in mice the pyridine derivative

was shown to protect against haemolytic streptococcus infection in smaller doses than cephalosporin C.

L. P. Garrod

BRODHAGE, H. & STOFER, A. R. **Polyoxymethyleneurea, a New Type of Locally Applicable Chemotherapeutic Agent.** *Antibiotics & Chemotherapy.* New York. 1961, Mar., v. 11, No. 3, 205–6.

"PP 1 is a colorless polyoxymethyleneurea insoluble in water, that is distinguished by good bacteriostatic action in vitro against Gram-positive and Gram-negative bacteria. The determination of acute and chronic toxicity (oral) on guinea pigs and rats shows that PP 1, even in doses of 2,320 mg./kg. of body weight (acute) and 1,000 mg./kg. of body weight (chronic, for 9 weeks) respectively, has no toxic effect."

SEVAG, M. G. & ISHII, K. **Drug-Induced Reversible and Irreversible Enzyme Alterations Underlying Drug-Resistance.** *Proc. Roy. Soc.* Ser. B. 1958, July 1, v. 149, No. 934, 63–81, 2 figs. [17 refs.]

—— & YOKOTA, T. **Evolution of the Phenomenon of Drug-Resistance. II. Studies of the Extracellular and Intracellular Derivatives of Folic Acid in relation to Resistance to Sulphathiazole and Growth Factor Requirements.** *Ibid.*, 1960, Nov. 29, v. 153, No. 951, 205–19, 2 figs. [18 refs.] **III. The Origin of the Development of Resistance to Sulphathiazole in *Escherichia coli* and *Staphylococcus aureus*.** *Ibid.*, 220–33, 6 figs. (1 on pl.) [15 refs.]

CLAUBERG, K. W. **Versuche zum Ersatz der Dampfdesinfektion durch gezielt strömende Entkeimungsgase. II. Mitteilung: Apparatur zur Testung bakterizider Gase. Grundsatzerörterungen. [Studies of the Substitution for Steam Disinfection of Controlled-Flowing Bactericidal Gases: Part II. Apparatus for Testing Bactericidal Gases. Definition of Principles]** *Arch. f. Hyg. u. Bakt.* 1961, Mar., v. 145, No. 2, 153–60, 5 figs.

The author describes and illustrates with a detailed diagram a continuous insulated metal tunnel, furnished with a fan to keep the air constantly circulating, a heating coil, and means for raising the internal pressure and for introducing triethylene glycol. This has been used for determining the conditions necessary for killing vegetative bacteria (only staphylococci are mentioned by name, and spores have yet to be studied) with triethylene glycol vapour. No details of the method are given although it is mentioned that strain variations in resistance and variations in the composition of triethylene glycol (which is liable to contain other glycols) have caused difficulty. A good deal is said about the rate of flow in the tunnel and means of measuring it. The actual results reported simply relate killing time to temperature (on which apparently the glycol content of the atmosphere depends), rate of flow and pressure. The last-named had no effect [there is no apparent reason why it should *per se*]: the results of the other tests showed that a temperature of 100–110°C. and a flow rate of 2·5–5 metres per second were adequate. There were apparently no similar studies on the effect of humidity. Mattresses are mentioned as objects which can probably be better disinfected in this sort of way than by steam.

[For Part I see this *Bulletin*, 1961, v. 36, 180.]

L. P. Garrod

BACTERIA

The order in this section is:—**Cocci; Donovania; Mycobacterium; Corynebacterium; Haemophilus; Pseudomonas; Pfeifferella; Enteric Organisms; Brucella; Pasteurella; Bacillus; Anaerobes; Spirochaetes; Erysipelothrix; Listeria; Others.**

JOHNSON, J. E., 3rd.; CLUFF, L. E.; GOSHI, K.; CONTI, C. R. **Studies on the Pathogenesis of Staphylococcal Infection. I. The Effect of Repeated Skin Infections** [JOHNSON, CLUFF & GOSHI]. *J. Exper. Med.* 1961, Feb. 1, v. 113, No. 2, 235–48, 1 fig. on pl. [24 refs.] **II. The Effect of Non-Specific Inflammation** [GOSHI, CLUFF, JOHNSON & CONTI]. *Ibid.*, 249–57. [17 refs.] **III. The Effect of Tissue Necrosis and Antitoxic Immunity** [GOSHI, CLUFF & JOHNSON]. *Ibid.*, 259–70, 3 figs. on 3 pls. [18 refs.]

I. Rabbits were injected intradermally with dilutions of a living suspension of staphylococci. Only the low dilutions produced lesions. The rabbits were further challenged with the same doses at weekly intervals, and it was found that progressively higher dilutions produced pustular lesions. Skin tests with a killed vaccine revealed the development of cutaneous hypersensitivity; there was, however, very little detectable circulating antibody. 2 rabbits were given injections of heat-killed staphylococci in Freund's adjuvant and subsequently challenged with living staphylococci; they responded like the rabbits that had had repeated challenges with living cocci, suggesting that sensitization was responsible for the increased susceptibility. The previously infected rabbits also differed from controls in a greater susceptibility of pyarthrosis after intra-articular injection of

staphylococci and in lower degree or severity in the hypopyon induced by injection into the anterior chamber of the eye.

II. The depilated skin of rabbits was injured by burning and by treatment with croton oil. During the first day, or 3 days in the case of burning, the damaged skin showed increased susceptibility to the intradermal injection of staphylococci. Later injection of staphylococci revealed no enhanced susceptibility. Inflammation produced by group A streptococci did not significantly enhance the staphylococcal lesion, nor did that associated with the Arthus reaction or the tuberculin reaction.

III. The injection of 10^4 staphylococci into a necrotic burn on the rabbit skin produced an extensive local lesion, though even 10^7 cocci injected into the normal skin produced only a small pustule. The infected burns eventually healed without scarring. On repetition of the burning and injection of staphylococci into the burn, there was little or no sign of infection, although these rabbits developed identical lesions to those of previously uninfected rabbits after intradermal inoculation in normal skin. The animals that had recovered from infected burns had high titres of antibody to alphatoxin. Protection against the infection of necrotic burns could be induced by active immunization with toxoid, or by passive transfer of serum from an actively immunized animal. This protection was not type-specific.

It seems, therefore, that the susceptibility of rabbits to staphylococci infection can be increased by repeated infections—by a phenomenon similar to sensitization—and by some forms of tissue damage. In the first case infection is not affected by active immunization with toxin or toxoid; in the latter it is prevented by such immunization. *R. E. O. Williams*

JUNGERMAN, D. **Investigations on the Antigen Structure of *Staphylococcus aureus*.** *Bull. Acad. Polonaise des Sci.* Warsaw. Sér. Sci. Biol. 1961, v. 9, No. 1, 15–20, 4 figs. on pl. [14 refs.]

A scheme for the fractionation of staphylococci is outlined and was applied to 4 strains of *Staph. aureus*. Agar cultures of the organisms were disrupted by the freeze-thaw method and 7 fractions were prepared, 5 by extraction of cell mass and 2 by precipitation of the supernatant fluid.

Each of these fractions were subjected to chemical analysis for nitrogen, phosphorus, carbohydrate, DNA and ribose by standard methods and to chromatographic analysis for sugars, amino-acids and fatty acids.

Although disruption of all strains was not uniform, the separated fractions showed only minor differences between strains. Lipoprotein-polysaccharide; nucleoprotein and polysaccharide fractions were obtained. All lipoprotein fractions contained fatty acids and the same amino acids that were found in the nucleoprotein fractions. These findings are compared with the findings of other workers. *M. Patricia Jevons*

JUNGERMAN, D. **Immunochemical Properties of Intracellular Antigens of *Staphylococcus aureus*.** *Bull. Acad. Polonaise des Sci.* Warsaw. Sér. Sci. Biol. 1961, v. 9, No. 1, 21–4.

Staphylococci fractions prepared as described in the previous paper were studied by complement-fixation and double-diffusion tests against unabsorbed rabbit antisera. The sera were prepared by injection of heat-killed, followed by living organisms and animals were bled when a suitable titre was reached [how this was assessed is not stated].

In the complement-fixation tests graded doses of the various fractions were titrated against a constant dose of serum and complement. Results are not given in detail but nucleoprotein fractions and one of the polysaccharide fractions fixed complement. Reactions were not specific for sera or antigens.

The polysaccharide fraction which fixed most complement was also most active as judged by the gel-diffusion technique, producing 2–3 bands of precipitation. Nucleoprotein fractions failed to precipitate.

Amongst the fractions which showed precipitation there were numerous cross-reactions.

M. Patricia Jevons

MILCH, Hedda. **Isolation of New *Staphylococcus* Phages and their Use in Phage Typing.** *Acta Microbiologica.* Budapest. 1960, v. 7, No. 4, 419–32, 2 figs. [25 refs.]

The author describes 4 new staphylococcus phages obtained from lysogenic cultures of *Staphylococcus aureus* from routine hospital material in Hungary. 2 of the phages (304 and 377) belong to serological Group A and 2 (756 and 950) to serological Group B. By means of these 4 phages the number of untypable strains was decreased from 28·8% to 15·9%. The lytic spectra of these phages on routine material showed 3 of them to be Group III phages and 1 (304) to be a miscellaneous phage. [It would be helpful if workers describing new and locally useful phages could give the lytic spectra of these phages on the internationally accepted set of test strains. The strains are used in all national centres for testing preparations of the basic set of phages and are readily available. Action of new phages on these strains may provide a better basis for comparison with other phages than their action on local strains.]

M. Patricia Jevons

MARSTON, Judith. **Observations on L Forms of Staphylococci.** *J. Infect. Dis.* 1961, Jan.–Feb., v. 108, No. 1, 75–84, 10 figs. [10 refs.]

L colonies of staphylococci were produced in 48 hours at 37°C. from 8 penicillin-sensitive strains after inoculation into brain heart infusion agar containing added NaCl (5%), heat inactivated normal horse serum (20%) and crystalline penicillin G (1,000 units/ml.). The L colonies of all strains reproduced on transfer to plates of the same medium; after several such transfers they

reproduced on the same medium without penicillin. A broth medium similar in all components, except agar, to that used for production and maintenance of L forms proved unsuitable for continued cultivation of these forms. However, when the broth was supplemented with as little as 0·1% agar it proved suitable for maintenance and possibly allowed multiplication of the L forms.

Inoculation of L colonies into agar medium fortified with yeast extract (4%) but devoid of penicillin and horse serum and containing a lower salt concentration (2·5%) resulted in the appearance of cocci after incubation for 7–8 days. The reverted cocci were found to be of the same bacteriophage pattern as the original inoculum, where phage types were demonstrable, and in addition were penicillin sensitive. The sensitivity patterns of the recovered cocci, to all other antibiotics tested, were similar to those of the original inoculum. [In contrast see this *Bulletin*, 1960, v. 35, 388.]

H. Gooder

SALL, T., MUDD, S. & TAUBLER, J. **Concerning the Surfaces of Cells of Staphylococcus Pyogenes. I. A Pseudocapsulation Phenomenon under Certain Experimental Conditions.** *J. Exper. Med.* 1961, Apr. 1, v. 113, No. 4, 693–700, 18 figs. on 4 pls. [22 refs.]

This paper describes a staphylococcus of phage type 42B/52/80/81 which, when grown on a yeast extract tryptone medium containing 3% gelatin, 5% Noble agar, 3·3% lactose and 3·3% mannitol, produces an extracellular material that can be revealed in india ink preparations and by various electron-micrograph techniques. A variant of the strain, which failed to produce free coagulase and fibrinolysin, also failed to produce the extracellular material. This material is thought to be different from the mucoid capsule described for the "Smith" strain and is referred to as a pseudocapsule.

R. E. O. Williams

OMORI, G., KATO, K. & IIDA, S. **The Lysozyme Test in the Study of Staphylococci associated with Food Poisoning.** *Osaka City Med. J.* 1960, v. 6, No. 1, 33–8.

The relationship between coagulase and lysozyme production in staphylococci isolated from food was investigated. Of 325 strains tested, 120 produced free and bound coagulase, and lysozyme. 2 produced bound coagulase and lysozyme but no free coagulase. Of 203 strains which produced no coagulase of either sort only 3 produced lysozyme.

An outbreak of food poisoning involving 40 victims was investigated and strains of similar biochemical properties were isolated from 3 patients and 1 dish of food (phage typing was not done). These strains produced lysozyme but no free coagulase and spontaneous agglutination prevented the identification of bound coagulase. Injection into kittens of the heat-killed supernatants of cultures incubated in Dolman's medium produced vomiting.

The authors point out that enterotoxin-producing strains of staphylococci may therefore be coagulase-negative and in such cases it may be useful to test for the production of lysozyme. *M. Patricia Jevons*

RAJCHERT-TRZPIL, Marianna. Wpływ podłóż, temperatury i areacji na wytwarzanie hialuronidazy przez gronkowce. **[The Effect of Media, Temperature and Aeration on the Production of Hyaluronidase by Staphylococci]** *Med. Dośw. i Mikrobiol.* Warsaw. 1961, v. 13, No. 2, 97–104, 1 fig. [24 refs.]

The English summary appended to the paper is as follows:—

"It was found that increased aeration of a culture possesses a great influence on the production of hyaluronidase by staphylococci. This is expressed by manifold increase of the amount of produced hyaluronidase in aerated cultures in comparison with the amount in stationary cultures.

"The type of medium used also plays an important role. The production of hyaluronidase was stimulated by a factor present in the yeast extract, different from thiamine because the addition of thiamine did not effect the amount of produced enzyme.

"The experiments concerning the influence of temperature on the production of hyaluronidase have shown that the optimal temperature is 30°C. At this temperature the maximum amount of hyaluronidase is obtained after 24–30 hours.

"Comparing correlation for coagulase and phosphatase production to hyaluronidase production—the following was found: for coagulase-positive and phosphatase-positive strains the coefficient of correlation amounted to 0·91; for coagulase-positive and phosphatase-negative—0·33; for coagulase-negative and phosphatase-positive—0·87. The examined coagulase-negative and phosphatase-negative strains did not produce hyaluronidase.

"These results would indicate that the property of producing hyaluronidase is correlated with the production of phosphatase rather than that with coagulase."

BUNGAY, Celia. **The Effect of Temperature on the Production by Coagulase-Positive Staphylococci of Staphylokinase and other Extracellular Substances.** *J. General Microbiol.* 1961, Mar., v. 24, No. 3, 393–400, 2 figs. [18 refs.]

Growth of 3 coagulase-positive strains of staphylococci at a temperature higher than 35°C. resulted in a progressive and marked diminution in the yields of staphylokinase and hyaluronidase. The total mass of growth and the yields of both α-haemolysin and the Panton-Valentine leucocidin were unchanged. Between 35°C. and 43°C. staphylokinase production decreased by 18% per mgm. dry weight of organisms for each degree rise in temperature. The amount of hyaluronidase produced per mgm. dry weight of organisms was 5 to 8 times greater at 37°C. than at 41°C. *H. Gooder*

RITZERFELD, W., KIENITZ, M. & GLODNY, H. Über Beziehungen zwischen Atmungsaktivität, Hämolysinbildung und Enterotoxinproduktion bei Staphylokokken. [**The Relation between Respiratory Activity, Haemolysin Production and Enterotoxin Production by Staphylococci**] *Ztschr. f. Hyg. u. Infektionskr.* 1960, v. 147, No. 2, 144–57, 3 figs. [38 refs.]

26 strains of *Staph. aureus*, thought on clinical or laboratory evidence, or both, to produce enterotoxin, were compared with 14 strains thought not to produce enterotoxin, for their oxygen uptake during growth in a Warburg apparatus. [The laboratory tests actually used for determining the enterotoxin production are not stated.] Almost all the presumed enterotoxin-producing staphylococci showed a higher oxygen consumption at the end of the log phase of growth than did the control strains. There was also some indication that the enterotoxin-producing strains produced more α-haemolysin.

R. E. O. Williams

WALLMARK, G. & FINLAND, M. **Phage Types and Antibiotic Susceptibility of Pathogenic Staphylococci. Results at Boston City Hospital 1959–1960 and Comparison with Strains of Previous Years.** *J. Amer. Med. Ass.* 1961, Mar. 11, v. 175, No. 10, 886–97, 5 figs. [18 refs.]

The phage type and antibiotic sensitivity of 1,550 strains of *Staph. aureus* isolated from clinical lesions of patients in the Boston City Hospital between 1950 and 1960 were determined. Over these years strains of Group I (mainly 80/81 group of strains) increased at the expense of the Group III strains. Strains of Group II were most frequent among paediatric cases and the 80/81 group of strains was more frequent from patients on surgical wards.

There were only 3 strains of Type 80/81 and related types in the first 2 years of the study. In the last 3 years 45% of strains from in-patients were of Group I and about half of these were of the 80/81 group and 60% of strains from out-patients were Group I with a similar preponderance Type 80/81. There was an increase in non-typable strains from in-patients and these tended to be antibiotic-resistant.

There was a continued slight increase in the resistance of strains to penicillin, tetracyclines and streptomycin and a marked increase in resistance to chloramphenicol, erythromycin and novobiocin during the period of study and there was a relationship between the proportion of antibiotic-resistant strains and the length of stay in hospital. More strains from patients who had received antibiotics were more resistant than those from patients who had not been so treated, but the resistance of individual strains was not necessarily resistance to the drug the patient had received. The evidence suggests that the increase in resistant organisms is due to the elimination of sensitive strains permitting the establishment and multiplication of resistant strains.

[For an earlier study, see this *Bulletin*, 1960, v. 35, 1031.]

M. Patricia Jevons

STEWART, G. T., with the technical assistance of R. J. HOLT & Jean A. WHITE. **Changes in Sensitivity of Staphylococci to Methicillin.** *Brit. Med. J.* 1961, Mar. 25, 863–6, 2 figs. [17 refs.]

During 13 transfers on media containing increasing concentrations of methicillin, 3 strains of *Staphylococcus aureus* showed little increase in resistance (from *nil* to 5-fold), but 4 strains of *Staph. albus* showed increases of 5-, 10-, 20- and 400-fold: these changes were accompanied by lesser degrees of increase in resistance to penicillin G, but there was no demonstrable penicillinase formation to account for this resistance. Increases in resistance to methicillin during and after treatment were also seen in 3 cases of *Staph. albus* septicaemia. On the other hand, in 2 similar cases (infection of a Spitz-Holter valve) due to *Staph. aureus* no increase in resistance to methicillin was seen after treatment for 5 and 8 weeks, nor was it seen in re-isolations after treatment of other *Staph. aureus* infections, in 12 cases from the lesion and in 20 from the nose. Nasal swabs were taken from patients and staff before and weekly during a 12-week period of spraying a ward with methicillin: no resistant strains of either species of staphylococcus were recovered. These encouraging results "do not support" the view that methicillin "should be kept in reserve for difficult staphylococcal infections lest more widespread use should lead to acquisition of resistance. . . ." (An editorial (p. 886) takes a less optimistic view, and points out that penicillin G is preferable to methicillin on several grounds for treating staphylococcal infections unless they are resistant to it.)

[See also this *Bulletin*, 1961, v. 36, 173.]

L. P. Garrod

WOLFE, M. D. & CAMERON, G. M. **Fluorescent Antibody Technique versus Cultural Methods as a Routine Procedure for finding Beta-Hemolytic Streptococci in Throat Cultures.** *Pub. Health Lab.* 1959, July, v. 17, No. 4, 76–82.

"A total of 722 throat cultures were examined for the presence of Group A streptococci utilizing the fluorescent antibody technique and for the presence of beta-hemolytic streptococci by routine cultural methods.

"The fluorescent antibody technique was more sensitive, by the methods used, on specimens that contained only a few Group A organisms.

"In 98·1 per cent of the specimens giving positive results with the labelled streptococcus Group A antiglobulin, no fluorescence occurred with labeled normal globulin.

"In 1·9 per cent of the specimens giving positive results with the labeled streptococcus Group A antiglobulin, fluorescence also occurred with labeled normal globulin. This was theorized as probably being caused by specific staphylococcus antibodies in the rabbit serum, due to previous exposure to the organisms. Staphylococcus cultures were isolated from four of these specimens representing phage types 77, 7/83, and 7. These organisms gave typical fluorescent reactions with both the labeled 'normal' conjugate and labeled Group A conjugate. One of these gave a reaction in the precipitin test with Group A antiserum

when the test was performed at the Communicable Disease Center (Moody-1959).

"Absolute proof that these staphylococcus reactions are due to exposure of the rabbit to these staphylococci prior to immunization rather than to cross reactions is still lacking. However, the fact that only one of these organisms reacted with the Group A streptococcus antiserum in the precipitin test is substantiating evidence.

"The fluorescent antibody technique proved to be a more simple test to perform, a more economical test, and a more rapid test providing for quicker reports of results to the physician."

REDYS, J. J., ROSS, M. R. & BORMAN, E. K. **Inhibition of Common-Antigen Fluorescence in Grouping Streptococci by the Fluorescent Antibody Method.** *J. Bacteriology*. 1960, Dec., v. 80, No. 6, 823–9. [14 refs.]

Difficulties were experienced in obtaining group-specific, streptococcal antiserum conjugated with fluorescein isothiocyanate suitable for the rapid identification of Group A streptococci present in throat swabs [this *Bulletin*, 1958, v. 33, 1083]. In order to overcome this difficulty a technique depending on the inhibition of common antigen fluorescence among serological groups A, C and G was developed. The technique consisted of transferring portions of the streptococcal suspension (derived from an overnight broth culture of an isolated colony) to 2 adjacent areas on a glass slide. The smears were air dried and heat fixed. A drop of unlabelled Group C antiserum (at a predetermined dilution) was applied to one of the encircled smears and blotted off after 5 minutes. Fluorescein-labelled Group A antiserum was then applied to both smears and the staining completed in the conventional manner. The comparative intensity of staining of the paired smears was then determined and if no reduction in intensity was observed in the smear treated with Group C antiserum, the specimen was adjudged to contain Group A streptococci.

In a 3-month period 4,480 throat swabs were received, of which 1,256 (28%) yielded haemolytic streptococcal colonies on blood agar. A representative colony was transferred to broth and, after incubation, the subsequent growth was tested by the precipitin method for group specific carbohydrate and by the fluorescent staining method. 934 of the isolated organisms contained Group A antigen and they all gave a positive staining reaction. No positive staining was observed with any of the remaining cultures.

Attempts to stain smears of organisms prepared from single colonies obtained from the primary isolation plates were unsuccessful. Inoculation of throat swabs directly into broth medium, which had been rendered selective for streptococci by the addition of inhibitory agents, showed that successful identification of Group A streptococci by the staining technique was possible, provided reasonable numbers of streptococci were present in the inoculum. If blood agar plates inoculated in parallel with the selective broth grew fewer than 10 haemolytic colonies then positive staining results were not found. [In the reviewer's laboratory it has usually been possible to prepare group-specific fluorescein-labelled streptococcal antiserum by the method previously described (*ibid., loc. cit.*). Occasional rabbits have produced the difficulties described in this present paper.] *H. Gooder*

QUINN, R. W. & MARTIN, Margaret P. **The Natural Occurrence of Hemolytic Streptococci in School Children. A Five-Year Study.** *Amer. J. Hyg.* 1961, Mar., v. 73, No. 2, 193–208, 5 figs. [11 refs.]

The studies by QUINN and his colleagues on the carriage of haemolytic streptococci in healthy school-children attending one or other of 3 schools in Nashville, Tennessee, during the 5-year period 1953–58 are continued [this *Bulletin*, 1957, v. 32, 1195].

There was considerable yearly fluctuation in the number of positive swabs obtained from the 3 schools from year to year but the overall carriage rate was not significantly different from the 3 schools (20·2%–23·1%). An average of 24 swabs per year per child were taken in the years 1953–54 and 14 swabs per year per child subsequently. Of these 66% of the positive cultures had more than 10 colonies per plate. There were no consistent seasonal differences in carriage rate. No epidemics of streptococcal disease occurred and there were no cases of glomerulonephritis but there was 1 case of rheumatic fever.

The study is based on 12,323 cultures, of which 1,596 strains were serologically grouped and 84·3% belonged to Group A but only 33% of these could be typed with M antisera. The most common types were 1, 6, 12, 4 and 3 and the type distribution changed in each school from year to year.

Classroom space and ventilation were similar in the 3 schools and there was no evidence that the carriage rate was higher in the more crowded homes, or those with other children. There was, however, some indication that, except in the first year of the study when carriage rate was high, children with tonsils had significantly higher streptococcal carriage rates than those without tonsils. *M. Patricia Jevons*

ROTTA, J. & RASKA, K. Průběh infekce u králíků po intraperitoneální implantaci komůrky s kulturou A-streptokoků. **[The Course of Infection in Rabbits after Intraperitoneal Implantation of Chambers containing Culture of Group A Streptococci]** *Československ. Epidemiol., Mikrobiol., Imunol.* Prague. 1961, v. 10, No. 3, 176–83, 1 fig.

The English summary appended to the paper is as follows:—

"Streptococci in broth culture in a chamber with walls produced of membrane filter (Sartorius No. 7, mean size of pores 175 millimicrons) implanted into the peritoneal cavity of the rabbit remain alive for more than nine months. Although the membrane filter is impermeable in vitro, when the chamber is implanted into the peritoneal cavity of the rabbit (in vivo) minute quantities of streptococci penetrate into the organs of

the animals, and in a relatively high percentage of cases long-term, clinically inapparent persistence of the micro-organisms in the organs ensues. Only exceptionally rabbits die from general streptococcal sepsis in the first weeks after the implantation. If, however, a killed streptococcal group A culture, of identical or different type, is repeatedly injected into the rabbits prior to the implantation of the chamber, a marked change in the animals' reactivity occurs: a large part of the animals (60%) succumb within a few days after the implantation. Animals thus sensitized that survive the implantation of the chamber produce antistreptolysin O more frequently and in higher titres than control animals. Long-term persistence of streptococci in the animals has been detected even at a time when live streptococci have no longer been found in the implanted chambers."

ROBERSON, B. S. & SCHWAB, J. H. **Endotoxic Properties associated with Cell Walls of Group A Streptococci.** *J. Infect. Dis.* 1961, Jan.–Feb., v. 108, No. 1, 25–34, 4 figs. [33 refs.]

Cell walls of a Group A streptococcus (D58) [probably type 3 not type 1 as stated] were prepared by disruption of the organisms in a sonic disintegrator. Purified suspensions were obtained by differential centrifugation, digestion with papain and sedimentation through sucrose gradients. These preparations, in doses of 1 to 2 mgm., had pyrogenic activity, produced a transient leucopenia and leucocytosis in rabbits, prepared rabbit skin for a Shwartzman reaction, altered the reaction of rabbit skin to adrenalin and were lethal for mice and rabbits. Further treatment by sonic vibration reduced the effective pyrogenic dose to 100 μgm. which is vastly greater than the pyrogenic dose of 0·002 μgm. per kgm. reported for the lipopolysaccharide endotoxins obtained from Gram-negative bacteria [WESTPHAL and LUDERITZ, *Angew. Chem.*, 1954, v. 66, 407].

These endotoxic responses, induced by components derived from cell walls of a Group A streptococcus, are ascribed to their non-specific macromolecular properties of size and composition and appear unrelated to the specific and distinctive capacity of those components to produce a chronic remittent lesion of connective tissue [this *Bulletin*, 1960, v. 35, 694].

H. Gooder

PETERSEN, K. F.; KRÖGER, H.; ROTTHAUWE, H. W. Untersuchungen über die Streptokokken-Diphosphopyridinnucleotidase. I. Partielle Reinigung und Charakterisierung des Enzyms. **[Investigations of Streptococcal Diphosphopyridine Nucleotidase. I. Partial Purification and Characterization of the Enzyme]** [PETERSEN, KRÖGER & ROTTHAUWE]. *Ztschr. f. Hyg. u. Infektionskr.* 1961, v. 147, No. 4, 350–56, 1 fig. [24 refs.] II. Reaktionskinetische Studien, Entwicklung von Methoden zum Enzymund Antikörper-Nachweis. **[II. Studies of the Reaction Kinetics; Development of Methods for demonstration of Antibodies]** [PETERSEN]. *Ibid.*, 357–68, 8 figs.

(L. 390)

I. The supernatant fluids from cultures of Group A streptococci were fractionated with ammonium sulphate and yielded a 6-fold concentration of streptococcus diphosphopyridine nucleotidase.

II. The partially purified enzyme was tested for its temperature and *p*H optima and a test was devised for the estimation of the antibody to diphosphopyridine nucleotidase in human sera. Details of the test must be sought in the original. *R. E. O. Williams*

SPAUN, J., BENTZON, M. W., LARSEN, S. O. & HEWITT, L. F. **International Standard for Antistreptolysin-O.** *Bull. World Health Organization.* Geneva. 1961, v. 24, No. 2, 271–9.

In its second report, the WHO Expert Committee on Rheumatic Diseases (1957) recommended the establishment of an international standard for human antistreptolysin-O [this *Bulletin*, 1957, v. 32, 1155]. The present paper records the collaborative work, in 12 laboratories, which has led to the definition of the International Standard.

Serum, for the proposed standard preparation, was obtained from 3 patients with streptococcal infection. The samples were pooled, freezed-dried, and sealed under vacuum. On reconstitution the serum was found to remain stable at −15°C., and 4°C., and 20°C. and +37°C. for at least 4 weeks.

10 laboratories participating in the main study investigated 8 single serum samples obtained from different patients and two samples of the proposed standard by means of the technique and with the streptolysin O normally employed by them. In addition, a series of tests was performed with a single preparation of streptolysin O supplied to all participants. The results indicated that when a standard serum was used the values obtained by different laboratories were reasonably comparable and that adjustment of the various streptolysin O preparations by means of the standard serum rendered the values obtained in the same laboratory, at different times, more nearly equal. Values were also obtained from a comparison of the proposed standard with that of the current Danish standard, the units of which corresponded to the unit originally defined by TODD [IPSEN, *Acta. Path et. Microbiol. Scandinavica*, 1944, v. 21, 203]. The mean value was then assigned to the proposed International Standard. Two further laboratories then made a direct comparison between the proposed standard globulin preparation established by Todd. [This latter preparation is used as a reference standard by many laboratories in the United Kingdom.] The mean value of 9 comparisons was within 5% of the value assigned to the proposed International Standard. The International Standard is defined, on a weight basis, as 0·0213 mgm. of the lyophilized pooled serum. [It is available in the fluid state in ampoules containing 10 International Units per ml. from the appropriate regional laboratory of Biological Standards.]

H. Gooder

SEIFERT, H. Die Bestimmung des Hämolysehemmtiters im Verein mit der Antistreptolysinreaktion. **[Determination of the Haemolysis Inhibition Titre in connexion with the Antistreptolysin Reaction]** *Ztschr. f. Immunitätsf. u. Exper. Therap.* 1960, Dec., v. 120, No. 5, 314–25.

An apparent increase in serum antistreptolysin titres (AST) was found on storage of haemolytic sera. To reproduce this effect an artificial haemolysis was produced in normal serum samples by the addition of graded amounts of completely autolysed blood clots. The highest dilution of the autolysed blood cells which did not immediately increase the AST was defined as the haemolysis inhibition titre (HHT). On storage the AST of the haemolysed red-cell-serum mixture increased. The HHT of 20 serum samples varied from 1:6 to 1:50,000. Pairing of sera derived from blood groups, A_1, A_2, B and O with homologous or heterologous macerated blood clots did not influence the HHT. [The role of cholesterol, which, when free or bound to red cell stroma is a potent inhibitor of oxygen-labile haemolysins should be considered. See for example COHEN *et al.* (this *Bulletin*, 1942, v. 17, 886).] *H. Gooder*

TAUBER, H. & RUSSELL, H. **Biochemistry of *Neisseria gonorrhoeae* Endotoxin.** *Bull. World Health Organization.* Geneva. 1961, v. 24, No. 3, 385–6.

LYON, R. H., LICHSTEIN, H. C. & HALL, W. H. **Factors affecting the Growth of *Mycobacterium tuberculosis* in Aerobic and Stationary Cultures.** *Amer. Rev. Respiratory Dis.* 1961, Feb., v. 83, No. 2, Pt. 1, 255–60, 5 figs. [12 refs.]

Investigations by many workers have indicated that inadequate diffusion of oxygen is responsible for the arithmetic linear growth of mycobacteria in liquid culture. In the present study, with inocula from 7-day cultures and by measuring the increase in growth in a spectrophotometer, the authors showed that although aeration by rotating the flasks at 140 r.p.m. did not affect the growth of H37Rv and H37Ra in Dubos media, it markedly increased growth in Sauton and Kirchner media; in contrast, aeration increased the growth of *Mycobacterium ranae* in all 3 media.

Aerating the media for 4 days before inoculation had no effect on the growth, and *p*H and Eh measurements revealed no significant differences between aerated and non-aerated cultures. However, exchanging the carbohydrate components of the media shows that it was the glucose of Dubos medium that was mainly responsible for the failure of aeration to stimulate growth; when glycerol was substituted for the glucose, aeration stimulated growth. *S. R. M. Bushby*

OSCARSSON, P. N. **Investigation of Catalase and Peroxidase Activity of Löwenstein Cultures. Relationship between Enzyme Activity, Isoniazid Susceptibility and Guinea-Pig Tests.** *Acta Tuberculosea Scandinavica.* 1961, v. 40, No. 1, 51–64. [29 refs.]

The purpose of this investigation was primarily to show whether catalase and peroxidase tests could forecast the isoniazid resistance of freshly isolated strains of tubercle bacilli. 386 strains growing on Löwenstein medium were tested by the simultaneous method of WARFVINGE (*Nordisk. Med.*, 1957, v. 58, 1395) for detecting the 2 enzymes. Repeat tests, up to 5 times, of 163 cultures gave varying results with almost 50% of these strains but as more consistent results were obtained from homogenous cultures, these variable results were probably due to heterogenicity of the cultures.

In strains with positive tests for both enzymes more than 90% were subsequently shown to be sensitive to 0·2 μgm. isoniazid per ml., and of the strains giving negative reactions for these tests, 75% were more resistant (inhibited by not less than 1 μgm. isoniazid per ml., and more than 50% by 50 μgm. per ml. or more). No correlation was found between enzyme activity and susceptibility to aminosalyl and streptomycin.

[This is a very involved paper, containing a mass of figures, and readers especially interested in this aspect of the subject are recommended to consult the original article.] *S. R. M. Bushby*

NAGASUGA, T., TERAI, T. & YAMAMURA, Y. **Studies on the Toxic Lipid of Isoniazid-Resistant Human Tubercle Bacilli.** *Amer. Rev. Respiratory Dis.* 1961, Feb., v. 83, No. 2, Pt. 1, 248–54. 1 fig. [18 refs.]

A strain of (attenuated) tubercle bacilli resistant to 50 μgm. isoniazid per ml. was grown in Sauton medium for 4 weeks and then autoclaved. The bacilli were collected, twice extracted with an ether-methanol mixture at 0°C. for 2 days and then with chloroform for 4 days. The chloroform extract was concentrated and ether added to it; the wax was then precipitated with methanol. This purified wax was fractionated into the C and D waxes by either acetone or benzene-acetone mixture extraction. Chromatographic separation on magnesium-silicate—infusorial-earth yielded a toxic fraction from both the C and D waxes, representing 6·3% and 26·7%, respectively, of each.

This toxic fraction was also isolated by chemical extraction methods from the purified wax, and toxicity studies showed that 0·005 mgm. of the fraction killed mice within 10 days. The fraction was shown by infra-red spectroscopy, melting point and elementary analysis to be identical with the cord factor of virulent tubercle bacilli, and as the yield was similar to that reported from the virulent bacilli, the authors concluded that there is no correlation between levels of virulence and the cord factor content of tubercle bacilli.

S. R. M. Bushby

FODOR, T. Die Wirkung von Zymosan auf die experimentelle Meerschweinchen-Tuberkulose. [**The Action of Zymosan in Experimental Tuberculosis in Guineapigs**] *Zent. f. Bakt.* I. Abt. Orig. 1961, v. 182, No. 1, 93–5.

The English summary appended to the paper is as follows:—

"Infection tests in guinea pigs showed a remarkable increase in the severity of a tuberculous infection, if tubercle-bacilli were admixed with Zymosan. In intramuscular infections the addition of Zymosan resulted in a much higher degree of tuberculous changes within the same time period and with the same number of tb.-bacilli than in control groups without Zymosan."

MURASE, T. **Studies on Tuberculopolysaccharide Fractionated with Resin Chromatography (Ecteola-Cellulose)—its Chemical and Biological Properties.** *Nagoya J. Med. Sci.* 1961, Mar., v. 23, No. 4, 343–61, 8 figs. [56 refs.]

SHEPARD, C. C. & KIRSH, D. **Fluorescent Antibody Stainability and other Consequences of the Disruption of Mycobacteria.** *Proc. Soc. Exper. Biol. & Med.* 1961, Apr., v. 106, No. 4, 685–91, 4 figs. [14 refs.]

"1) Mycobacteria were broken open by vibration with glass beads. Ninety to 95% of the protoplasm, and 70–80% of the bacterial mass was released into a soluble state and could be separated by centrifugation from the sediment (disrupted bacilli), which consisted largely of cell walls. 2) Intact bacilli of the 5 more slowly growing species studied were not stainable with fluorescent antibody, but disrupted bacilli stained brightly. This was interpreted as evidence that the outer surfaces of intact bacilli of these species are free of antigen. 3) Intact bacilli of 3 of the more rapidly growing species stained well. 4) The soluble fraction contained the greatest amount of antigen as judged by ability to inhibit staining of the disrupted bacilli. It could be used to absorb (inhibit) cross-reacting antibodies to render immune sera more specific in their staining of disrupted organisms. 5) The soluble fraction was a potent antigen in agar diffusion tests. In complement fixation tests it was also an effective antigen with helpful specificity."

LARSON, C. L., RIBI, E., WICHT, W. C. & LIST, R. **Skin Reactions produced in Rabbits by Cell Walls and Protoplasm of *Mycobacterium tuberculosis* and *M. butyricum*.** *Amer. Rev. Respiratory Dis.* 1961, Feb., v. 83, No. 2, Pt. 1, 184–93, 3 figs. [17 refs.]

In a previous paper [this *Bulletin*, 1958, v. 33, 1176], the authors showed that cell walls but not protoplasm of *Mycobacterium butyricum* and *Myco. tuberculosis* produce lesions and induce hyper-sensitivity when injected into rabbits. The present paper emphasizes these differences and shows that the hypersensitivity induced by the cell walls also extends to the protoplasm.

The bacilli were grown in Dubos medium and after being washed they were disrupted in either a Mickle apparatus or a pressure cell. The cell walls and protoplasm were separated by differential centrifugation and the protoplasm preparations were shown to be free of cell walls by electron micrography. The preparations were sterilized with 0·4% formalin, 0·5% phenol or by heating at 75°C. for 45 minutes.

Approximately 1 μgm. of cell wall material injected intradermally into rabbits produced an indurated red area of 5 mm. or more in diameter in 4–5 days, which persisted for 4–5 weeks, whereas 100 μgm. of protoplasm produced transient erythema and oedema, fading in 24 hours. 2·5 μgm. of cell walls of *Myco. butyricum* or 10 μgm. of those of the tubercle bacillus produced hypersensitivity of the delayed type to cell walls, protoplasm and tuberculin, lasting at least 44 days. The factor in the cell wall responsible for hypersensitivity was resistant to treatment with ether, formalin, phenol or heat, and it did not appear to have suffered by the extraction process for the walls were at least as active as heat-killed untreated bacilli. The ability of the cell wall to induce hypersensitivity was also demonstrated in guineapigs. *S. R. M. Bushby*

TIMOŞCA, Sofia & STAVRI, Natalia. Rezistența la infecția cu *Mycobacterium tuberculosis* a cobailor sensibilizați prin transferul celular al alergiei tuberculinice. [**Resistance to *Mycobacterium tuberculosis* Infection in Guineapigs sensitized by Cellular Transfer of Tuberculin Allergy**] *Microbiol., Parazitol., Epidemiol.* Bucharest. 1961, Mar.–Apr., v. 6, No. 2, 127–34, 3 figs. [12 refs.]

The English summary appended to the paper is as follows:—

"Passive transfer of allergy from tuberculous to healthy animals was obtained by the aid of peritoneal exudate cells, thus confirming the data in literature concerning the cellular support of allergy. A further comparative study was carried out on the behaviour of guinea pigs sensitized in this way and those which had received virulent inoculation with tubercle bacilli.

"Experiments showed that the sensitivity conferred to guinea pigs by means of peritoneal exudate cells from tuberculous animals seemed to aggravate the course of tuberculosis."

TAKAHASHI, Y. & ONO, K. **Study on the Passive Hemagglutination Reaction by the Phosphatide of *M. tuberculosis*. I. The Reaction and its Specificity.** *Amer. Rev. Respiratory Dis.* 1961, Mar., v. 83, No. 3, 381–5. **II. Conditions of the Reaction.** *Ibid.*, 386–93.

I. "The phosphatide of *M. tuberculosis* is capable of sensitizing normal sheep erythrocytes to hemagglutination in the presence of tuberculous serum. The antigen-antibody system participating in the phosphatide hemagglutination is completely independent of that participating in the polysaccharide hemagglutination."

II. "The antigen-to-saline drop method was found to be the best method for the preparation of antigen emulsions suitable for the passive hemagglutination reaction by the phosphatide of tubercle bacilli. Ordinary saline or buffered saline at pH 7·0 and 8·0, prepared by adding 1/10 volume of phosphate buffer at respective pH values, was found suitable for obtaining the reaction.

"The sensitization of erythrocytes and the reaction of the mixtures of antigen and sensitized erythrocytes took place satisfactorily at 37°C. for thirty minutes. Of the complement-fixation, precipitation, and hemagglutination tests, the last-named gave the highest antibody titers. Upon addition of complement, the phosphatide hemagglutination reaction was converted to the hemolytic reaction, giving still higher antibody titers."

JANICKI, B. W. & PATNODE, R. A. **Increase in Circulating Lysozyme-Like Enzyme following Sensitization of Guinea Pigs with *Mycobacterium tuberculosis*.** *Amer. Rev. Respiratory Dis.* 1961, June, v. 83, No. 6, 872–7. [23 refs.]

TACQUET, A., TISON, F. & DEVULDER, B. Action bactéricide du yaourt sur les mycobactéries. **[Bactericidal Activity of Yoghourt against Mycobacteria]** *Ann. Inst. Pasteur.* 1961, May, v. 100, No. 5, 581–7.

Suspensions of 4 strains of human type *Mycobacterium tuberculosis* when added to yoghourt (fresh or autoclaved) were killed in 24 hours. BCG was killed in 48 hours, but an avian strain and 2 atypical mycobacteria survived. Reasons are given for concluding that this bactericidal effect is not due to nisin, nor is it a pure *p*H effect: HCl at *p*H 4·2 (that of yoghourt) was not lethal. A simple solution of lactic acid in distilled water having the same *p*H was not lethal, but one containing 0·36% each of the D− and L− forms of lactic acid, brought to *p*H 4·2 with soda, had the same lethal effect as yoghourt itself. *L. P. Garrod*

ENGBAEK, H. C. & MAGNUSSON, M. **A Bacteriological Study of the Pathogenic Significance of Atypical Mycobacteria isolated from Eleven Patients.** *Acta Tuberculosea Scandinavica.* 1961, v. 40, No. 1, 1–34, 8 figs. [45 refs.]

This report is concerned with 11 patients from whom atypical mycobacteria were isolated; all of the patients had signs and symptoms of pulmonary disease but tubercle bacilli were isolated from only 2 of them, and atypical mycobacteria were isolated on more than 1 occasion from 9. The report includes case histories of the patients and bacteriological details of the strains, including pathogenicity for guineapigs, rabbits, mice and hens. All except 1 of the patients were over 40 years of age, and there was no evidence that they had developed the infections from contact or that they had transmitted the infection to other persons.

Two of the strains were orange-coloured, unaffected by light and non-pathogenic to animals, but 1 of these was considered to be definitely pathogenic for th patient; they were considered to be *Mycobacteriu scrofulaceum*. 6 of the strains were non-photochr mogenic and 3 of these were pathogenic to the rabb and mouse; they were considered to be pathogen for the patients and to be either *Myco. avium* or the Battey type. The 3 other strains were no pathogenic and their presence in the patients w considered to be incidental. The remaining 3 strai were rapidly-growing mycobacteria and although th case histories of the patients do not suggest that the were pathogenic, they may have contributed to th disease through the resistance of the patient havi been reduced by corticotrophin treatment; these strains were considered to belong to the species *Myc fortuitum*. Comparative Mantoux tests with huma and avian tuberculins and sensitins from the homol gous strains showed that at least 3 of the 4 patients f whom the strains were pathogenic had been sensitize with the strains, and that the other strains had had n sensitizing effects. Experiments in guineapigs confirme that the injection of the bacilli sensitized the animals t the homologous sensitin of the atypical mycobacteri and therefore reaction in the patient could be expecte to disclose an infection with the strain in question.

[This is an extensive and detailed paper. Th histories of 2 of the patients and much of the informa tion on cross-sensitivity reactions between the strain of atypical mycobacteria and other mycobacteria hav been reported earlier (this *Bulletin*, 1958, v. 33, 389 1960, v. 35, 184).] *S. R. M. Bushby*

ENGBAEK, H. C. **Pathogenicity and Virulence o Atypical Mycobacteria for Experimental Animal with particular reference to Pathological Pro cesses in the Joints and Tendon Sheaths o Rabbits.** *Acta Tuberculosea Scandinavica.* 1961 v. 40, No. 1, 35–50, 1 fig. on pl. [17 refs.]

These studies were stimulated by the observatio that 3 of the strains of the previous paper [above] an avian-like strain and 2 Battey-type strains, had pro duced pathological changes in the joints and tendo sheaths of rabbits. In the present study the strain examined were 8 avian strains, 10 strains of *Myco bacterium kansasii*, 4 scotochromogens, 8 Battey-typ strains, 7 other Runyon type III strains, 3 Runyon I strains, 12 strains of human tubercle bacilli, 6 bein resistant to isoniazid, 2 strains of bovine tubercl bacilli, 1 being resistant to isoniazid. The bacilli wer injected intravenously into rabbits, intravenously an intraperitoneally into guineapigs, and intravenously int hens and mice.

Involvement of the joints and tendon sheaths, bu to varying degrees, occurred with 9 of the strains o *Myco. kansasii*, 7 of the Battey strains and with onl 1 of the other type III strains; all of these strains wer considered to have been pathogenic for the patie from whom they were isolated. Of the other strain examined, only the tubercle bacilli, especially thos with reduced virulence, produced similar lesions. I the joint lesions, the capsule and often the tendo sheath, protruded and contained gritty viscous fluid o a grey to yellowish colour; the synovial membrane wa

often swollen and numerous necrotic foci were visible in the bone-ends.

The results of the virulence tests in mice in general paralleled those in the rabbit, especially with the *Myco. kansasii* strains, but the mouse seemed to be the most sensitive experimental animal for the scotochromogens. The hens died spontaneously after intravenous injection of 5 mgm. of the *Myco. kansasii* strains and only occasionally after infection with the other atypical mycobacteria. *S. R. M. Bushby*

TÁRNOK, I. Serologische Aktivität der Mycobakterien-Desoxyribonucleinsäuren. [**Antigenicity of Mycobacterial Deoxyribonucleic Acids**] *Zent. f. Bakt.* I. Abt. Orig. 1961, v. 182, No. 1, 96–105, 3 figs. [24 refs.]

The English summary appended to the paper is as follows:—

"1. DNA of low protein content isolated from mycobacteria gives a complement fixation reaction with rabbit immune sera prepared with homogenized mycobacteria.

"2. Deoxyribonuclease treatment induces a partial, and, in one experiment, a total inhibition of the complement fixing ability.

"3. Protein decomposing enzymes do not influence the complement fixing ability of DNA.

"4. The immune sera tested gave cross reactions with DNA preparations with other saprophytic mycobacteria, but not with nucleic acids isolated from M. ranae, calf thymus, rabbit or guinea pig organs.

"5. The possible causes of the phenomena observed are discussed. It is stressed that a nucleic acid-protein complex may be responsible for the antigenicity of DNA."

GALE, D. **Studies of Unclassified Mycobacteria. I. *In vivo* Response and Morphologic Studies of a Photochromogen.** *Amer. Rev. Respiratory Dis.* 1961, May, v. 83, No. 5, 718–27, 1 fig.

KUBICA, G. P.; VESTAL, Annie L.; BEAM, R. E.; RIGDON, A. Louise. **The Arylsulfatase Activity of Acid-Fast Bacilli. I. Investigation of Activity of Stock Cultures of Acid-Fast Bacilli** [KUBICA & VESTAL]. *Amer. Rev. Respiratory Dis.* 1961, May, v. 83, No. 5, 728–32. [12 refs.] **II. The Differentiation of *Mycobacterium avium* from the Unclassified Group III Nonphotochromogenic Mycobacteria** [KUBICA & BEAM]. *Ibid.*, 733–6. **III. Preliminary Investigation of rapidly growing Acid-Fast Bacilli** [KUBICA & RIGDON]. *Ibid.*, 737–40.

RYBICKA, Irena & KUDELSKI, Z. O właściwościach antyhemolitycznych toksyny i anatoksyny błoniczej. [**The Anti-Haemolytic Properties of Diphtheria Toxin and Anatoxin**] *Med. Dośw. i Mikrob.* Warsaw. 1961, v. 13, No. 2, 117–25. [10 refs.]

The English summary appended to the paper is as follows:—

"The aim of the study was to investigate the ability of combining of diphtheria anatoxin with the antibodies present in the blood of rabbits immunized by means of guinea pigs blood cells and to explain whether this reaction can be used in routine work on the assessment of the immunologic value of diphtheria vaccine. Ninety experiments were carried out, 48 series of mono- and polyvalent anatoxins of Polish and foreign make were examined.

"The following conclusions were drawn: 1) Diphtheria anatoxin, whether it is the only constituent of the vaccine or enters into the composition of a combined vaccine, may possess the ability of combining with the agglutinating and hemolyzing antibodies of the guinea pig blood cell. 2) No correlation was found between the immunizing power of diphtheria anatoxins ascertained by biological experiments on guinea pigs by routine methods and the ability of combining with the hemolytic serum. The anatoxins possessing good immunogenic properties may combine with the hemolysins but these properties may be absent as well. 3) The factor present in the diphtheria vaccines combining with the hemolytic serum of a rabbit seems to be a different type than factor immunizing animals or human being. 4) The anti-hemolytic factor probably appears when adequate media for culturing of Corynebacterium diphtheriae are employed for the purpose of obtaining toxin."

STRÍZOVÁ, V., RASKOVÁ, H., VANĚCEK, J., with the technical assistance of M. DRÁBOVÁ, B. RYBOVÁ & O. FIALOVÁ. K farmakologii pertusového toxinu. Sdělení I. [**A Contribution to the Pharmacology of the Pertussis Toxin. 1st Communication**] *Československ. Epidemiol., Mikrobiol., Imunol.* Prague. 1961, v. 10, No. 3, 192–6, 4 figs.

The English summary appended to the paper is as follows:—

"The raw thermolabile toxin of B. pertussis causes a slowly developing constriction of bronchae. The rate of the constriction is essentially increased in animals sensitized with the toxin.

"In a number of isolated smooth muscles, a slow contraction is caused by the toxin. Relatively often, the isolated gut of a guinea pig is sensitized for histamin, by the toxin, and the isolated uterus of a rat is sensitized for acetylcholine."

YAMADA, K. **Studies on Pseudomonas Phage (Phage Typing for Pseudomonas).** *Mie Med. J.* Tsu. 1960, Nov., v. 10, No. 3, 359–65. [16 refs.]

"1) Phage typing was made of 34 kinds of Ps. aeruginosa, isolated and by this typing, Ps. aeruginosa was classified into 6 kinds of types.

"2) On the basis of this classification, 6 kinds of strains of Ps. aeruginosa were selected as the type strains which are possibly used for phage typing method.

"3) Comparative studies of classification by phage typing and serological typing method revealed that

both kinds of classification were almost the same as each other."

JAMESON, J. E. **A Study of Tetrathionate Enrichment Techniques, with particular reference to Two New Tetrathionate Modifications used in isolating Salmonellae from Sewer Swabs.** *J. Hygiene.* 1961, Mar., v. 59, No. 1, 1–13.

This paper compares the efficiency of 3 tetrathionate enrichment media, a standard preparation, a combination of tetrathionate broth and the ingredients of the Wilson and Blair medium and a combined medium containing sodium lauryl sulphate. This last named medium was similar to the other combined medium except that the Wilson and Blair ingredients were present in half the concentration and there was the added sodium lauryl sulphate in a concentration of 1%. The reasons underlying the use of sodium lauryl sulphate were that preliminary experiments with salmonella-infected animal feeding stuffs had indicated that culture media containing this compound supported the growth of salmonellae at incubation temperatures in the region of 44°C., whereas strains of *Proteus*, at this temperature, failed to grow.

The comparative trial of the three media for the enrichment of sewer swab specimens in a village investigation of an outbreak of Salmonella Heidelberg infection was undertaken with the hope that the results would be sufficiently clear-cut to indicate which medium was superior for enrichment purposes. This was not achieved, for the assessment of the different enrichment media was complicated by a number of factors. Although the incorporation of sodium lauryl sulphate in the medium yielded satisfactory results in that the richest growths of salmonellae were obtained with this medium it did not always yield the greatest number of salmonella isolations.

The investigation revealed a number of interesting points and the original paper should be consulted for details of these as they cannot easily be abstracted.

H. J. Bensted

ANDERSON, E. S. **Slime-Wall Formation in the *Salmonellae*.** [Correspondence.] *Nature.* 1961, Apr. 15, v. 190, 284–5.

A characteristic property of *Salmonella paratyphi B* is the formation of slime-wall in cultures which, after normal incubation at 37°C., have been allowed to stand on the bench for 24 hours or more; cultures of *Salm. paratyphi B* var. *Java* do not exhibit this property. The usual method of demonstrating slime-wall formation is to incubate plate cultures on nutrient agar for 18–24 hours at 37°C. and then to keep these at 20–25°C. for a further period of 24 hours when the colonies will show the characteristic appearance.

This preliminary communication records a deeper study of the phenomenon and draws attention to the fact that a nitrogen-free polysaccharide containing more than 40% glucose, present in the cultures showing slime-wall formation, is constantly associated with its demonstration. The concentration of phosphate in th culture medium has an important influence on th synthesis of the polysaccharide and the author, usin Sörensen buffer *p*H 7·0 as the source of phosphat found that strains of *Salm. paratyphi B* not showin slime-wall formation or fermentation of D-tartrate whe grown on ordinary nutrient agar developed the pow to form slime-wall and to ferment D-tartrate whe grown on phosphate-agar. The maximal effect w obtained with Sörensen buffer in a concentration M/5 added to Difco agar. It was noted that mo strains of paratyphoid B organisms isolated from cas of enteric fever formed slime-wall on ordinary ag media but the majority of the strains of this organis isolated from cases of food-poisoning showed slime-wa formation only when grown on phosphate-agar. few enteric fever strains also required the presence phosphate in the agar medium for obvious slime-wa formation.

The property described is not restricted to par typhoid B organisms but all salmonellae and certa other members of the Enterobacteriaceae family w form slime-wall on agar media containing suitab concentrations of phosphate. The synthesis of th polysaccharide depends on aerobic conditions of grow and a *p*H of 6·5 or more (optimum 7·0) of the pho phate medium. The addition of 0·5% glucose w found to increase slime-wall formation but was n essential for the synthesis of the polysaccharid Other sources of phosphate may be employed but th Sörensen buffer is very suitable. It is not yet know whether the polysaccharide of which slime-wall formed is identical in all the salmonellae or oth groups of organisms showing slime-wall formation the presence of high phosphate-concentrations, but th and other related problems together with certa immunological aspects are being studied.

[As a preliminary contribution this paper ha considerable interest.] *H. J. Bensted*

COLOBERT, L. & KIRN, A. Les propriétés lytiques d sérum normal. II. Obsistine et antigène V d'*Eberthella typhi*. **[Lytic Properties of Norma Serum. II. Obsistin and Vi Antigen of *Ebe thella typhi*]** *Ann. Inst. Pasteur.* 1961, Feb., v. 10 No. 2, 159–65, 4 figs.

The sensitivity of Gram-negative bacteria to the lyt action of obsistin [this *Bulletin*, 1961, v. 36, 311] variable and among the salmonellae it is found tha some serotypes are lysed and others are not; there ma also be differences in varieties of the same main ser type. This paper is concerned with the difference sensitivity to obsistin of *Salmonella typhi* O–901, whic does not carry the Vi antigen, and a strain of typho bacilli with the full complement of Vi antigen. Whi the O-agglutinable Vi-negative O–901 strain is lysed b obsistin the O-inagglutinable Vi-positive strain is resis ant to its action and it is concluded that this resistan is due to the protective envelope of the complete V antigen. This protective effect of the surface antige is discussed in relation to the bacteraemia in typho fever. *H. J. Bensted*

UCZOWSKI, Z. **Experiments on Biochemical and Phage Typing of *Salmonella paratyphi* A.** *Bull. Inst. Marine Med. Gdańsk.* 1960, v. 11, Nos. 3/4, 101–8. [11 refs.]

Using the 5 BANKER-phages of *Salmonella paratyphi* [this *Bulletin*, 1955, v. 30, 720] the author examined st over 200 strains of *Salm. paratyphi A* which had een isolated at various times—up to 6 years previously. lost of these cultures represented single cultures from atients but in a proportion there were two or more om the same patient. When the phage typing experi- ents on each culture were repeated the great majority ave concordant results, but in some cases significant fferences were observed either with regard to phage nsitivity or to H_2S production. Over 75% of the ltures showing concordant results belonged to phage- pe 1, just over 1% were type 3 and about 2% were sensitive to the phage preparations used; all these ere H_2S negative. Nearly one-fifth failed to show ecific sensitivity to the 5 phages and this was chiefly ith the phages 4 and 5 and these were grouped as olyvalent types; most of these were H_2S positive. In some of the cases where several cultures from ie same patient were available the results were fficiently irregular to cast doubt on the epidemio- gical value of phage typing of this organism. It is ot known, however, whether these cultures represented ngle colony isolation or a mixed culture of ten or ore colonies, as is generally recommended.

H. J. Bensted

AN OYE, E. Étude de l'antigène O:27 des Salmonellae. [**Study of *Salmonella* Antigen O:27**] *C.R. Soc. Biol.* 1960, v. 154, Nos. 8/9, 1656–7.

This is in the nature of a preliminary communication bout the position of the B-group salmonella O ntigen:27. The author found that organisms in is group carrying O:27, when heated for $2\frac{1}{2}$ hours t 125°C., lost their power to evoke the production of gglutinins for O:27 and also their agglutinability by pure O:27 antiserum but they still retained their ower to absorb O:27 antibody. Unlike O antigen:5, owever, antigen 27 resisted the action of N/1 HCl. t is suggested that antigen 27 may not be a true antigen since this partial heat lability is similar o that found in some of the surface antigens and it ight be more proper to regard it as a K antigen. urther studies are in progress and the author would refer to await the results of these before accepting s confirmed the observations he has already recorded.

H. J. Bensted

GUINÉE, P. A. M. & KAMPELMACHER, E. H. **A New *Salmonella* Type (S. Benguella).** *Antonie van Leeuwenhoek: J. Microbiol. & Serol.* 1961, v. 27, No. 1, 31–2.

"A new *Salmonella* type of *S. benguella*, with the ntigenic formula 40:b:z_6, is described. The culture vas isolated together with *S. meleargridis* from fishmeal f Portuguese Angola origin."

VAN OYE, E., VAN ROS, G. & HERMAN, F. Une nouvelle espèce de *Salmonella* en provenance du Congo: Salmonella Kivu (6,7:d:1,6). [**A New Species of *Salmonella* isolated in Congo: Salmonella Kivu 6,7:d:1,6**)] *Ann. Inst. Pasteur.* 1961, June, v. 100, No. 6, 812–13.

JANDL, G. Die Herstellung eines polyvalenten *Salmonella*-Serums. [**Preparation of a Polyvalent Salmonella Antiserum**] *Ztschr. f. Hyg. u. Infektionskr.* 1960, v. 147, No. 1, 38–49. [15 refs.]

The author discusses the preparation and testing of a polyvalent salmonella diagnostic antiserum for slide agglutination. The antiserum was prepared by immunizing rabbits with a pooled suspension of 25 salmonella strains, which were washed off agar plates with 1% formol saline. The strains included *Salmonella paratyphi B, paratyphi C, bovis morbificans,* Albany, *typhi,* Berta, Panama, *anatum,* Lexington, Aberdeen, Poona, Carrau, Szentes, Kirkee, Cerro, Monschaui, Weslaco and Niarembe, all in flagellar phase 1, and 7 other salmonellae in flagellar phase 2, *viz.* Salmonella Bispebjerg, Amersfoort, Taksony, Worthington, Pomona, Donna and Allandale. The pooled suspension was diluted to a density of 10·8 thousand million organisms per ml., and this in turn to 2 vaccines containing 5×10^9 and 2×10^9 organisms per ml. respectively. Rabbits were immunized against these vaccines by a schedule of 5 injections with 48-hour intervals between successive doses, and were bled out 3 days after the final dose. The polyvalent antisera thus obtained, when fortified with various monovalent sera against a number of salmonellae that gave poor slide agglutination in preliminary tests, gave satisfactory slide agglutination with a series of 49 salmonella serotypes covering all the known salmonella antigens.

B. Moore

MICHAEL, J. G. & LANDY, M. **Endotoxic Properties of Gram-Negative Bacteria and their Susceptibility to the Lethal Effect of Normal Serum.** *J. Infect. Dis.* 1961, Jan.–Feb., v. 108, No. 1, 90–94. [10 refs.]

It has long been known that Gram-negative bacilli obviously deficient in O antigen, that is colonially rough cultures, are more sensitive to the bactericidal action of normal human serum than cultures of the same organism which were typically smooth. The present paper, however, deals with cultures of *Escherichia coli* and *Shigella dysenteriae* from which different colonies were selected on the strength of different opacity and refractivity but all had the typical characters of smoothness. The selected strains were then compared with regard to their antigenic and endotoxic properties in relation to their sensitivity to normal human serum. It was found that strains which were resistant to the bactericidal action of normal serum were more potent sources of somatic antigens and at the same time were richer in endotoxin than their serum sensitive counterparts. Qualitatively the

selected strains of the two groups possessed the same antigenic structure as judged by agglutination and absorption techniques. It is not known whether the difference between the strains in their complement of somatic antigens was sufficient for this to be detected by quantitative absorption procedures, but this is possible, of course, in the special case of colony selection of *Salmonella typhi* where the different opacities of the colonies can indicate varying complements of Vi antigen and this can be confirmed by quantitative absorption techniques. *H. J. Bensted*

ŠLOPEK, S. & MULCZYK, M. Lysotypie von *Shigella flexneri*. [**Phage Types of *Shigella flexneri***] *Zent. f. Bakt.* I. Abt. Orig. 1961, v. 181, No. 4, 478–81.

[See also this *Bulletin*, 1961, v. 36, 804.]

MACLEAN, F. I. & MUNSON, R. J. **Some Environmental Factors affecting the Length of *Escherichia coli* Organisms in Continuous Cultures.** *J. General Microbiol.* 1961, May, v. 25, No. 1, 17–27, 7 figs. [17 refs.]

"The lengths of organisms of *Escherichia coli* B/r grown in continuous culture in a glucose salts medium were measured over a wide range of population densities at 22° and 37°. In some cases the cultures were exposed to continuous gamma radiation at dose rates of 600 r./hr. at 22° and of 1000 r./hr. at 37°. The average length of the forms and the distribution with respect to length depended upon the temperature, population density and radiation dose rate. The growth rate was almost independent of population density over the range in which the average length of organism showed such a marked dependence. No significant differences in growth rate were observed as between unirradiated and irradiated cultures. Changes in average length of organisms are regarded as phenotypic responses to changes in growth conditions, some conditions favouring division and others inhibiting division amongst short organisms."

CARO, L. G.; FORRO, F., Jr.; **Localization of Macromolecules in Escherichia coli. I. DNA and Proteins** [CARO, L. G.]. *J. Biophysic. & Biochem. Cytol.* Baltimore. 1961, Mar., v. 9, No. 3, 539–53, 15 figs. [31 refs.] **II. RNA and its Site of Synthesis** [CARO & FORRO]. *Ibid.*, 555–65, 8 figs. [30 refs.]

LANDY, M., JOHNSON, A. G. & WEBSTER, M. E. **Studies on Vi Antigen. VIII. Role of Acetyl in Antigenic Activity.** *Amer. J. Hyg.* 1961, Jan., v. 73, No. 1, 55–65, 3 figs. [28 refs.]

Previous studies on the structure of the purified Vi antigen from *Escherichia coli* by this group of workers and their colleagues (see HEYNS *et al.*, *Chem. Berichte*, 1959, v. 92, 2435) have established the fact that consists of a highly polymerized acidic polysacchari made up of repeating units of N-acetyl d-galactosami uronic acid. Since acetyl groups constitute a conside able proportion of the polysaccharide it was decided determine, if possible, what part the acetyl grou played in antigenic and protective activity.

Acetyl groups were removed from the antigen l treatment with NaOH and it was found that the deacet lated antigen precipitated only 20–25% of the Vi an body in rabbit or horse antisera. Reacetylation wi ketene restored precipitative activity to 60–75% of th of the unaltered antigen. In the inhibition of Vi haer agglutination the deacetylated had only 1/400th of t activity of the untreated antigen; reacetylation restor this to about half the activity of the unaltered prepar tion. Mice immunized with either the deacetylated the reacetylated Vi antigen failed to show any appre able protective power against a virulent challenge *Salmonella typhi*, whereas in man a single injection the deacetylated antigen in a dose of 40 μgm. result in the development of Vi antibody to levels of the sam order as those produced by the untreated antigen.

H. J. Bensted

GROS, F., HIATT, H., GILBERT, W., KURLAND, C. G. RISEBROUGH, R. W. & WATSON, J. D. **Unstabl Ribonucleic Acid revealed by Pulse Labelling *Escherichia coli*.** *Nature.* 1961, May 13, v. 19 581–5, 9 figs. [19 refs.]

KAYSER, F. & PIERFITTE, M. Étude du métabolisme d acides nucléiques chez *Escherichia coli* sensible résistant à la sulfanilamide. [**Metabolism Nucleic Acids by *E. coli* Sensitive or Resistant Sulphanilamide**] *Bull. Soc. Chimie Biol.* 196 v. 43, No. 1, 143–52, 5 figs. [26 refs.]

BOEZI, J. A. & DE MOSS, R. D. **Properties of Tryptophan Transport System in *Escherich coli*.** *Biochim. et Biophys. Acta.* 1961, May 2 v. 49, No. 3, 471–84, 1 fig. [28 refs.]

BELLO, L. J., VAN BIBBER, Mary J. & BESSMAN, M. **The Enzymology of Virus-Infected Bacteri I. Demonstration of Two Forms of Deoxyguany late Kinase in Infected *Escherichia coli*.** *J. Bio Chem.* 1961, May, v. 236, No. 5, 1467–70, 3 fig [13 refs.]

ZIMMERMAN, S. B. & KORNBERG, A. **Deoxycytidin Di- and Triphosphate Cleavage by an Enzym formed in Bacteriophage-Infected *Escherich coli*.** *J. Biol. Chem.* 1961, May, v. 236, No. 1480–86, 7 figs. [24 refs.]

KORNBERG, S. R., ZIMMERMAN, S. B. & KORNBERG, A **Glucosylation of Deoxyribonucleic Acid h Enzymes from Bacteriophage-Infected *Esch richia coli*.** *J. Biol. Chem.* 1961, May, v. 23 No. 5, 1487–93, 4 figs. [18 refs.]

IMSANDE, J. **Pathway of Diphosphopyridine Nucleotide Biosynthesis in *Escherichia coli*.** *J. Biol. Chem.* 1961, May, v. 236, No. 5, 1494–7, 1 fig. [11 refs.]

MANDELSTAM, J. **Induction and Repression of β-Galactosidase in Non-Growing *Escherichia coli*.** *Biochem. J.* 1961, June, v. 79, No. 3, 489–96, 8 figs. [21 refs.]

JONES, K. M., GUEST, J. R. & WOODS, D. D. **Folic Acid and the Synthesis of Methionine by Extracts of *Escherichia coli*.** *Biochem. J.* 1961, June, v. 79, No. 3, 566–74, 4 figs. [19 refs.]

LION, M. B. & BERGMANN, E. D. **Substances which Protect Lyophilized *Escherichia coli* against the Lethal Effect of Oxygen.** *J. General Microbiol.* 1961, June, v. 25, No. 2, 291–6, 2 figs.

MUNSON, R. J. & MACLEAN, F. I. **The Nature and Radiation Sensitivity of the Long Forms of *Escherichia coli* Strain B/r.** *J. General Microbiol.* 1961, May, v. 25, No. 1, 29–39, 4 text figs. & 4 figs. on pl. [17 refs.]

"By suitable adjustment of growth conditions in continuous cultures, organisms of *Escherichia coli* B/r with average lengths covering a wide range were produced and studied. From X-ray survival data it was concluded that radiosensitive sites were distributed along the length of an organism at intervals of 1–1·5 μ, whilst nuclear staining by the HCl-Giemsa method showed chromatinic bodies at an average spacing of 1·2 μ. Thus each nuclear body appeared to be a radiosensitive site. Lysozyme treatment did not reveal evidence of transverse membranes apart from those at visible 'waists'. It was concluded that the longer organisms arose by the inhibition of the terminal stages of division. This inhibition did not affect the multiplication of the nuclear and cytoplasmic components, although there was considerable aggregation of nuclear material in irradiated organisms."

LINZ, R. & LECOCQ, E. Sur la réactivation d'*Escherichia coli* après traitement par les rayons ultraviolets. II. Photoréactivation des suspensions aqueuses de bactéries irradiées. [**Reactivation of *Escherichia coli* after Treatment by Ultraviolet Rays. II. Photoreactivation of Aqueous Suspensions of Irradiated Bacteria**] *Ann. Inst. Pasteur.* 1961 Feb., v. 100, No. 2, 180–89.

In previous articles the authors [see this *Bulletin*, 1961, v. 36, 602] have studied the reactivation of irradiated *Escherichia coli B* and K12 under certain conditions where the irradiated bacteria are transferred to broth culture media and incubated at 37°C.

If the suspension of irradiated bacteria is exposed to very low temperatures to produce instant freezing, photoreactivation is suppressed because of the absence of a fluid medium, but subsequent treatment by thawing and re-exposure to light at room temperature results in some reactivation. When variants of *E. coli* K12, resistant to streptomycin and tetracycline, which are also resistant to phages T4 and T6, are mixed together and first exposed to the action of ultraviolet light and then white light it will be found that a high proportion of the reactivated bacteria are resistant to both antibiotics but these organisms are resistant to the action of phage T6 only. This fact does not suggest that reactivation is the result of recombination of the irradiated bacteria.

H. J. Bensted

KAPLAN, H. S., SMITH, K. C. & TOMLIN, Patricia. **Radiosensitization of *E. coli* by Purine and Pyrimidine Analogues incorporated in Deoxyribonucleic Acid.** *Nature.* 1961, May 27, v. 190, 794–6, 3 figs. [22 refs.]

WIEDERMANN, G. & FLAMM, H. Antigengemeinschaft zwischen *Pseudomonas* und *Escherichia*. [**Common Antigenicity in *Pseudomonas* and *Escherichia***] *Zent. f. Bakt.* I. Abt. Orig. 1961, v. 182, No. 1, 67–70.

The English summary appended to the paper is as follows:—

"Absorption-tests show that E. coli 26:B 6 and some strains of Ps. pyocyanea possess the same O-antigens. The complex nature of this antigen is demonstrated by the fact that the coli-antigen O 26 counteracting serum is only partially neutralized by these Pseudomonas strains. Therefore the authors suggest that the Escherichia-attained antigen be named 26a, while the antigen which pertains to the Pyocyaneus strains be named 26b.

"The authors' results point out the importance of checking the appearance of the tested colonies whenever searching for pathogenic coli strains by means of the Gruber-Widal reaction. Early Pyocyaneus colonies gained from stool cultures which show neither pigmentation nor metallic gloss may, on account of this antigenic mutuality, be easily mistaken for Escherichia coli 26:B6."

EDWARDS, P. R., KAMPELMACHER, E. H., FIFE, Mary A. & GUINÉE, P. A. M. **Seven New Arizona Serotypes isolated from Reptiles.** *Antonie van Leeuwenhoek: J. Microbiol. & Serol.* 1961, v. 27, No. 1, 110–12.

"Seven new *Arizona* serotypes from snakes are described. The biochemical characteristics of the organisms were those of typical members of the *Arizona* group. The antigenic formulae of the types are 1, 4: 1, 6, 7; 1, 4: 1, 6, 7, 9; 5: 29: 25; 5: 33: 25; 24: 23: 31; 26: 32: 30; and 26: 33: 31. Attention is called to the antigenic relationships of the cultures to the *Salmonella* group."

SAKAZAKI, R., MURATA, M., FIFE, Mary A., EDWARDS, P. R. & ISHII, F. **Eight New Arizona Serotypes isolated from Reptiles with special reference to a New Arizona H Antigen.** *Japanese J. Med. Sci. & Biol.* 1960, Dec., v. 13, Nos. 4, 5 & 6, 169–72.

FIFE, Mary A., EDWARDS, P. R., SAKAZAKI, R., NOZAWA, M. & MURATA, M. **The Occurrence of Three Flagellar Phases in Arizona Serotypes.** *Japanese J. Med. Sci. & Biol.* 1960, Dec., v. 13, Nos. 4, 5 & 6, 173–8. [20 refs.]

ROUX, J. Virulence et toxicité des *Brucella.* [**Virulence and Toxicity of *Brucella***] *Rev. d'Immunologie.* 1961, Jan.–Mar., v. 25, Nos. 1/2, 32–45. [34 refs.]

This is more in the nature of a lecture or a review article than an account of original research.

The various aspects of virulence of the brucellae are considered and attention is drawn to the important fact that smooth strains of *Brucella* grow within the cells of the animal host and also can be shown to multiply intracellularly in tissue culture. Rough cultures will not multiply within the cells. In the host brucellae are essentially localized in the reticulo-endothelial system but the reaction to experimental infection will depend on the strain and the species of *Brucella* inoculated. Toxic fractions come from 2 sources: the cell wall lipid and the endoproteins. Toxic endoproteins are found only in virulent strains but the toxic substance from the cell wall does not depend on virulence and is found in all 3 species. These toxic lipids are antigenic and are associated with the development of the local cellular reaction following vaccination with the avirulent strain of *Br. abortus* S19.

The author draws attention to the development of the local lesion after vaccination as establishing evidence of immunity against brucellosis and indicates the similarity of the pathological processes in tuberculosis.

H. J. Bensted

WATANABE, Y. & HUZIWARA, T. L'effet inhibiteur des antibiotiques sur la multiplication de *Pasteurella tularensis* dans la culture tissulaire. [**Inhibition of Multiplication of *Br. tularensis* by Antibiotics in Tissue Culture**] *C.R. Soc. Biol.* 1960, v. 154, Nos. 8/9, 1690–93, 4 figs.

Cultures of dispersed HeLa cells in tubes were inoculated with a suspension of a virulent strain of *Brucella tularensis.* After 24 hours the medium was replaced with fresh medium containing different concentrations of antibiotics. After a further 24 hours' incubation Giemsa-stained preparations were examined, and the percentage of infected cells compared with that in an untreated culture: a line drawing shows appearances after the first and second days of incubation with respectively small groups of bacteria in the cytoplasm and (when growth was not inhibited) cells packed with them. As other workers have previously shown, streptomycin and kanamycin failed to prevent int cellular bacterial growth except in high concentratic whereas oxytetracycline, chloramphenicol, erythromy and leucomycin inhibited growth in concentrations li in excess of those inhibitory *in vitro,* suggesting t they can readily penetrate the cell. *L. P. Garroc*

MIZUHARA, M. & YAMANAKA, M. **The Cytochrome *Pasteurella tularensis.*** [Correspondence.] *Natu* 1961, June 10, v. 190, 1024–5, 2 figs.

PARNAS, J. L'épreuve esculinique dans le diagnostic la peste et de la pseudotuberculose. [**The Aescul Test in the Diagnosis of Plague and Pseud tuberculosis**] *Ann. Inst. Pasteur.* 1961, Ma v. 100, No. 5, 691–2.

The author, from Lublin, Poland, describes brie a test for separating *Pasteurella pestis* and *P. pseud tuberculosis* from other organisms, such as *Salmone* and *Brucella,* which may be isolated in the routi examination of rodents. The strain under examinati is seeded in broth containing 1% aesculin. Wh growth has occurred a drop of ferric chloride is adde In sterile control broth or in that containing bacte which do not attack aesculin, a thick white sedime appears. In positive control broth inoculated wi enterococci [and presumably from the 2 *Pasteure* species] the sediment is black. The test is rapid a clear-cut.

A table shows the result with 44 strains of *P. pseud tuberculosis* from 7 species of animal and 1 strain fro man and with 10 strains each of *P. pestis* from man a rat. All of these were ++ in the aesculin test. strains of 6 other species of *Pasteurella* from vario animals were negative, as were 17 strains of 6 speci of *Salmonella* and 10 of 3 strains of *Brucella. Prote OX19* (number of strains not stated) is shown as givi negative, + or ++. *H. J. O'D. Burke-Gaffney*

MOLLARET, H. H., with the technical collaboration M. C. DEPLANCHE. Contribution à l'étude d caractères biochimiques de *Pasteurella pseud tuberculosis* (bacille de Malassez et Vigna [**Contribution to the Study of the Biochemic Properties of *Pasteurella pseudotuberculos* (Malassez's and Vignal's *Bacillus*)**] *Ann. Ins Pasteur.* 1961, May, v. 100, No. 5, 685–90. [1 refs.]

This is a study of the effect of growth temperatu on some of the biochemical reactions of *Pasteurel pseudotuberculosis.* 327 strains of human and anim origin were tested—all serological groups I–V we represented, and a comparison was made with t reactions of 3 strains of *P. pestis* and 15 strains of *septica.* All reactions were tested at 18°C., 27°C., a 37°C. 318 of the 327 strains of *P. pseudotuberculos* split aesculin within 10 hours. *P. pestis* split it in le than 20 hours, but *P. septica* gave no reaction at a

Ability to grow on sodium citrate was tested on

media—Simmons citrate, Christensen's medium, and 1% citrate broth. *P. septica* and *P. pestis* did not grow at all. At 37°C. *P. pseudotuberculosis* did not grow, but at 18°C. most of the strains grew and caused a colour change in Simmons medium after 2 weeks. At 28°C. the growth was much slower. Similar results were obtained with the other media.

Fermentation of sodium malonate was positive for only serological type IV of *P. pseudotuberculosis*. Other serotypes, *P. pestis* and *P. septica* were negative. The reaction was strongest at 28°C. (48 hours), slower at 18°C. (4–7 days) and negative at 37°C.

None of the 3 species of *Pasteurella* fermented D-tartrate, L or I tartaric acids, produced lysine decarboxylase, tryptophan deaminase, or gave a positive phenyl pyruvic acid reaction at any of the temperatures tested. Neither *P. pestis* nor *P. pseudotuberculosis* grew in Braun's cyanide broth. 8 of 15 strains of *P. septica* did.

Ability to split urea was demonstrated on Ferguson's medium, urea-indole medium, Christensen's medium and urea placenta broth. All strains of *P. pseudotuberculosis* produced urease. The reaction was strongest at 37°C. and the most consistent results were obtained with placenta broth. *P. pestis* and *P. septica* had no urease.

These results confirm the value of the urease reaction to distinguish *P. pseudotuberculosis* from *P. pestis*, and that the fermentation of sodium malonate is peculiar to the serological type IV of *P. pseudotuberculosis*.

May F. McCallum

Mollaret, H. H. Contribution à l'étude de l'inoculation par voie oculaire de *Pasteurella pseudotuberculosis* (bacille de Malassez et Vignal). **[Contribution to the Study of Ocular Inoculation of *Pasteurella pseudotuberculosis* (Malassez' and Vignal's *Bacillus*]** *Ann. Inst. Pasteur.* 1961, June, v. 100, No. 6, 753–64. [24 refs.]

Matthews, A. D. & Karnauchow, P. N. **A Simple Technique for the Cultivation of Anaerobes.** *Canadian Med. Ass. J.* 1961, Apr. 8, v. 84, No. 14, 793–4, 3 figs. [10 refs.]

This is a modification of the pyrogallic acid and alkali technique; it is considered especially suitable for small bacteriological laboratories.

An inoculated plate and Eh indicator (BBL thioglycollate-resazurin) are put into a polythene bag. A screw cap containing a Seitz filter disc, 0·6–1·0 gm. powdered pyrogallic acid and 2 ml. of 50% aqueous solution of anhydrous sodium carbonate is also put into the bag. The bag is sealed with cellulose tape and placed in an incubator. This method is found to be efficient, fast, easy, clean and relatively inexpensive. The risks of contamination by the organisms and soiling by the chemicals are eliminated. The production of a CO_2 environment in a polythene bag is also being tested by the authors.

Norma Temple

Suri, J. C. & Rubbo, S. D. **Immunization against Tetanus.** *J. Hygiene.* 1961, Mar., v. 59, No. 1, 29–48, 6 figs. [24 refs.]

This paper is concerned with passive protection against tetanus with homologous and heterologous antitoxic sera and combined active and passive immunization in man and animals. Several observations of considerable interest were made with regard to the elimination of passive antitoxin. For instance, with rabbits passively immunized with horse tetanus antitoxin by the intravenous route in doses of 500 units per kgm. body weight the antitoxin level in the unsensitized animal fell to less than 1% of the initial after 10 days and in sensitized animals a similar loss was found after 7 days. In rabbits immunized subcutaneously the elimination was much more rapid in the sensitized animals than in the unsensitized and there was some evidence to indicate that no advantage was gained by increasing the dose of antitoxin. Similar results were obtained with mice and it is important to appreciate the profound loss of antitoxin in these rabbits and mice, whether normal or sensitized, from the 7th day onwards. The elimination of antitoxin in man showed a great deal of individual variation, but there was no significant evidence that sensitized persons eliminated subcutaneously administered antitoxin much more quickly than those not sensitized; 80–85% of both groups receiving 1,500 units antitoxin had protective levels after 7 days. The evidence regarding those receiving very large doses of antitoxin (10,000 units or more) is rather conflicting: some of the patients showed very rapid elimination of antitoxin irrespective of their previous experience of horse antitetanic serum.

Homologous antitoxin was immunologically superior to heterologous preparations in every respect both in animals and man. Elimination is slow; it persists in effective concentrations for at least 3 weeks; it can be used in low doses and therefore will not interfere with the primary response in combined immunization. The primary immune response is also not interfered with if adsorbed toxoid is given 7 or more days after the passive immunization of man with heterologous antitoxin, but the simultaneous injection of antitoxin and toxoid is not to be recommended, especially fluid toxoid, since this procedure in rabbits clearly interfered with the primary response and this was more marked with fluid toxoid than with adsorbed toxoid.

H. J. Bensted

Nikol'skaia, M. A. **Comparative Evaluation of the Efficacy of Intravenous and Intracarotid Injection of Tetanus Antiserum.** *J. Microbiol., Epidemiol. & Immunobiol.* London. 1960, v. 31, No. 6, 1108–14. [19 refs.] [Translated from Russian.]

The author reports that when rabbits were injected subcutaneously with a lethal dose of tetanus toxin and 48 hours later given 1,500 units of enzyme treated tetanus antitoxin by the intracarotid route 8 out of 10 recovered whereas with a similar preparation injected intravenously only 1 of 10 recovered. If another purified preparation of tetanus antitoxin, presumably

"salt concentrated" antitoxin was used, neither the intracarotid or intravenous route of injection was effective. Further experiments on rats with enzyme purified tetanus antitoxin labelled with ^{131}I showed that intracarotid injection resulted in the demonstration of significant amounts of antitoxin in both cerebral hemispheres but that after intravenous injection no antitoxin was demonstrated in either hemisphere. Confirmatory experiments with radio-active iodine solutions showed that, in spite of the relatively low permeability of the blood-brain barrier for iodides, considerably more gets through if the injection is *via* the carotid artery.

[The experiments described in this paper are of considerable interest and it may well be that intra-arterial injection is superior to intravenous injection since the injection of enzyme-treated tetanus antitoxin into the carotid artery, in an upward direction, makes available to the brain a greater amount of antitoxin than is obtained by the intravenous route. But further experimental work on the subject is obviously indicated.]

H. J. Bensted

Van der Hoeden, J., Szenberg, Esther & Evenchik, Z. **Leptospira-Agglutinating Factors in Turtle Sera.** [Correspondence.] *Nature.* 1961, Apr. 1, v. 190, 95–6.

While investigating wild animals in Israel for evidence of leptospirosis, the authors found that the sera of each of 58 swamp turtles (*Clemmys caspica*) agglutinated the Castellón and S102 strains of *Leptospira ballum* (representative of the complete and incomplete "biotypes"). The titres ranged between 1 in 250 and 1 in 32,000. Some of the sera (15 of 58) also agglutinated *L. hyos* but the titres were much lower (1 in 50 to 1 in 250). Negative results were obtained with the following serotypes of *Leptospira*: *icterohaemorrhagiae* and *sarmini* (which have some degree of antigenic relationship with *ballum*), *canicola*, *grippotyphosa*, *pomona*, *hebdomadis*, *sejroe*, *australis A*, *autumnalis* (Rachmat), *bataviae*, *poi*, and *mini* (Szwajizak).

None of the turtle sera agglutinated the following 4 strains of saprophytic water *Leptospira biflexa*: Sao Paulo, Patoc 1, Wa-Z, Wa-Leiden; but all of 35 of the sera tested did agglutinate a 5th strain, *L. biflexa-Gent*, and to about the same titres as *L. ballum*. *L. biflexa-Gent* and *L. ballum* have no common antigen.

Attempts to isolate leptospires from the viscera of turtles, by direct culture and by inoculation of hamsters, failed.

The following findings were obtained in further investigations of the active agent in the turtle sera. (1) All the agglutinating factor was present in the globulin fraction. (2) No agglutination occurred when distilled water was used for washing the antigen suspension and for diluting the sera: but the addition of 0·9% saline brought about immediate reaction to the original level. (3) Temperatures of 68–69°C. removed the agglutinating capacity of 12 turtle sera and 3 rabbit anti-*ballum* sera. (4) After freezing and thawing turtle sera, the concentration of agglutinating factor at the bottom of the tubes was × 20 that of the supernatant layer. (5) Agglutinin-absorption tests indicated that the turtle factor reacted as an agglutinin of the "incomplete" *ballum* type. (6) The *hyos* agglutinin was absorbed from turtle sera by *L. ballum*; but *ballum* agglutinins were not removed by absorption with *L. hyos*. No leptospires could be found in mice inoculated intraperitoneally with cultures of *L. ballum* to which small amounts of turtle serum had been added: control mice were regulraly infected with the *ballum* strains.

Attempts to immunize 3 turtles with *L. grippotyphosa* resulted in low agglutination titres (1/50–1/100).

Cross agglutinin-absorption tests of turtle sera with *L. ballum* and *L. biflexa-Gent* revealed that all "agglutinins," both homologous and heterologous, were removed. These results contrasted strikingly with those obtained with immune sera prepared from rabbits, guineapigs, and land tortoises (*Testudo graeca*) against *L. ballum* and *L. biflexa-Gent*: such sera contained only the homologous antibody and absorption with the heterologous strain failed to affect the titre of the homologous serotype. Moreover, no agglutinins for *L. biflexa-Gent* were found in the sera of hedgehogs naturally infected with *L. ballum* although these sera agglutinated *L. ballum* to significantly high titres.

Other workers [this *Bulletin*, 1959, v. 34, 334] have found leptospiral "agglutinins" in reptiles. Further work is needed to determine the origin and nature of the agglutinating and protecting factors just reported.

L. H. Turner

Imamura, S., Ashizawa, Y. & Nagata, Y. **Studies on Leptospirosis. I. Experimental Leptospirosis of Mice with Jaundice, Hemorrhage and High Mortality.** *Japanese J. Exper. Med.* 1960, Dec., v. 30, No. 6, 427–31, 2 figs.

Early workers found that mice, after inoculation with leptospires, usually became urinary carriers but failed to show symptoms or signs of infection. In 1941 Larson [this *Bulletin*, 1942, v. 17, 212] reported that mice 3 weeks of age were susceptible to infection with *Leptospira icterohaemorrhagiae*. Attempts to confirm these results, with Larson's strain of leptospire but a different strain of mice, failed in spite of various methods used either to enhance the virulence of the organisms or to interfere with the defence reactions of the young mice [Stavitsky and Green, *ibid.*, 1946, v. 21, 199].

The present authors found that laboratory-bred male mice (ddN strain of *Mus musculus*), 3 weeks of age and weighing 9–15 gm., were susceptible to *L. icterohaemorrhagiae* (Mikawashima strain) especially when young cultures (3 day) were used and hydrocortisone acetate was previously administered. Petechial haemorrhages were commonly found in the mice at autopsy especially in the lungs but also in subcutaneous tissue and lymph nodes. Jaundice was common, as was focal degeneration with loss of striation in skeletal muscle fibres.

[Inconsistencies between the details given in the text and those in the tabulated results detract from the value of this otherwise interesting paper.] *L. H. Turner*

Parnas, J., Koslak, A. & Krukowska, Maria. Leptospiren, die bei der Hausmaus (*Mus musculus*) auftreten. [***Leptospira* affecting the Common House-Mouse (*Mus musculus*)**] *Zent. f. Bakt.* I. Abt. Orig. 1961, v. 182, No. 1, 121–8, 2 figs. [11 refs.]

The English summary appended to the paper is as follows:—

"1,090 specimens of common house-mice (Mus musculus) collected in endemic districts of leptospirosis were examined by means of anatomic-pathologic, histopathologic, serologic, biologic and bacteriologic methods. The different methods of examination supplement each other. 53 common house-mice (4·86%) showed a positive serologic reaction. The following serologic types were found to be prevalent: L. grippotyphosa, L. sejroe, L. canicola, followed by L. australis B, L. saxkoebing, L. ictero-haemorrhagiae, L. mitis, L. pomona, L. australis A, L. autumnalis, L. bataviae, L. poi, L. hebdomadis, L. ballum.

"17 strains of Leptospira were isolated from common house-mice: L. grippotyphosa 12 times, L. sejroe 3 times, L. bataviae once, L. ictero-haemorrhagiae once.

"The authors are pointing out the importance of controlling the transfer of leptospirosis by common house-mice in regard to the epidemiology of leptospirosis."

Babudieri, B. & Dymowska, Z. Studien über einen polnischen Leptospira-Stamm der Serogruppe "Semaranga". [**Studies concerning a Polish Strain of *Leptospira* Belonging to the Serologic Group "Semaranga"**] *Zent. f. Bakt.* I. Abt. Orig. 1961, v. 182, No. 1, 129–34.

The English summary appended to the paper is as follows:—

"A strain of Leptospira which was isolated in the year 1948 in Poland, probably from a patients blood, was examined by serologic methods. The result of the tests disclosed, that the strain pertained to the serologic group 'Semaranga'. This strain, which is easily agglutinable by human Leptospira-positive or Leptospira-negative sera, is to be added to the group of water-Leptospira like the rest of the group 'Semaranga'."

Brill, J. & Polityńska, E. Die Differenzierung von *Erysipelothrix rhusiopathiae*-Stämmen mit Bakteriophagen. [**The Phage Types of *Erysipelothrix rhusiopathiae* Strains**] *Zent. f. Bakt.* I. Abt. Orig. 1961, v. 181, No. 4, 473–7. [15 refs.]

The English summary appended to the paper is as follows:—

"1. Two phage strains, designated F1 and F2 could be isolated, both being specific for serotype A of Erysipelothrix rhusiopathiae.

"2. All tested strains of serotype A of DEDIE proved to be sensitive to the test phages of type A.

"3. Strains of serotype B are resistant to test phages of type A. In two B strains latent phage A infection could be revealed by UV irradiation.

"4. Both the test phages F1 and F2 did not change their specific lytic properties during an observation time of four years.

"5. The type A specificity of the phage strains F1 and F2 characterises both these strains as test phages for the identification of phage type A."

BACTERIOPHAGES

Ralston, Doris J., Baer, Beatrice, Lieberman, Miriam & Krueger, A. P. **Virolysin, a Virus-Induced Lysin: its Appearance and Function in Phage-Infected Staphylococci.** *J. General Microbiol.* 1961, Mar., v. 24, No. 3, 313–25, 3 figs. [29 refs.]

Staphylococcus aureus K_1 cells infected with phages P_1 or P_{14} contain a lysin which is antigenically different from the autolysin of normal cells and which also differs in substrate and *p*H requirements [this *Bulletin*, 1957, v. 32, 1184]. Both virolysin and autolysin were assayed turbidimetrically by their lytic effect on heat-killed *Staph. aureus*, and they were distinguished by measuring the one in the presence of antiserum against the other. When samples of cocci infected with phage were chilled and lysed by tyrothricin at intervals during the phage growth cycle and the lysin content measured, the small amount of autolysin present was found to remain constant, whereas virolysin was first detected at 10–15 minutes when it started to increase linearly until the end of the latent period. The rate of premature lysis of infected cocci, and phage release, during the latent period depended upon their virolysin content.

The authors suggest that virolysin is concerned in the release of phage particles at the end of the latent period. A number of chemicals which inhibited the action of free virolysin on heat-killed cells also inhibited the lysis of infected cells and the release of phage at the end of the latent period. However, other factors also appear to be essential both for the lysis of infected cocci and for free virolysin to act. For instance, it did not lyse bacterial cell walls unless they had been altered in some way by phage particles or by heat, acetone or urea. Virolysin is apparently not concerned with the entry of phage material into the cocci after adsorption since it does not form part of the phage particle and can be separated from it by centrifugation.

Janice Taverne

KIESEWALTER, J. Über die Verwendbarkeit von Phage zur Diagnose analoger *Salmonella*-Gruppen. **[The Use of Phages for Group Identification of Salmonellae]** *J. Hyg., Epidemiol., Microbiol. & Immunol.* Prague. 1960, v. 4, No. 2, 166–70.

WASSERMANN and SAPHRA [this *Bulletin*, 1955, v. 30, 630] claimed to have found phages that acted specifically on different salmonella O antigens, thus permitting group identification of salmonellae by a phage typing procedure. The present author tested these phages on a collection of 197 Salmonella, 21 Arizona, 35 Shigella and 416 Escherichia strains and quite failed to confirm the original claims. The phage for group D did in fact lyse all group D strains but also lysed salmonellae of many other groups, and in addition 63 out of 532 non-Salmonella strains. The phages for groups B, C_1 and E did not even lyse all strains falling into these groups and also lysed other salmonellae and enterobacteria.

B. Moore

KOIBONG LI, BARKSDALE, L. & GARMISE, L. **Phenotypic Alterations associated with the Bacteriophage Carrier State of *Shigella dysenteriae*.** *J. General Microbiol.* 1961, Mar., v. 24, No. 3, 355–67, 1 text fig. & 4 figs. on 2 pls. [19 refs.]

Upon infection with phage T7, a rough mutant derived originally from *Shigella dysenteriae* Sh 136–T gave rise to nibbled colonies in which apparently the phage existed in a carrier state. The colonies were not lysogenic and the phage could be eliminated from them by growing the bacteria with T7 antiserum. On MacConkey plates, the mutant gave rise to both red and colourless colonies; phage was always associated with lactose-fermenting colonies and never with the colourless ones. Cells from lactose-fermenting colonies looked like spheroplasts under the microscope and were osmotically fragile.

Genetic experiments indicated that the mutant was in fact genotypically Lac^+ although phenotypically it was unable to ferment lactose unless associated with the phage. A cross between Lac^- *Sh. dysenteriae* and an Hfr strain of *Escherichia coli* which was also Lac^- gave rise to lactose-fermenting recombinants; as the *E. coli* strain was known to carry a deletion in the region of the chromosome controlling the formation of β-galactosidase the Lac^+ character must have been derived from the apparently Lac^- *Sh. dysenteriae* parent.

T7 forms a plaque with a halo and cells from the area of the halo have, it seems, been altered by an endolysin produced by the phage. Phage could not be isolated from the halo region and the cells there were immune to it, presumably because their receptors had been destroyed by the enzyme. The authors suggest that the phage endolysin acts on the surface of the cells to cause the phenotypic alteration, "unmasking" the genotype so that clones which were apparently unable to ferment lactose (or maltose or mannitol) acquire the ability to ferment them.

Janice Taverne

HRADECNÁ, Z. & MAZÁCEK, M. Eine Vergleichsstudie über die Eigenschaften nativer und getrockneter Bakteriophagen. **[Comparative Studies on the Properties of Dried and Untreated Bacteriophages]** *Zent. f. Bakt.* I. Abt. Orig. 1961, v. 181, No. 4, 469–72.

The English summary appended to this paper is as follows:—

"The electron microscopical morphology of dried and untreated Shigella flexneri and Shigella sonnei phages, their plaque size and their multiplication curve were compared. Drying as a process of the production of therapeutic preparations did not alter these properties of the phages."

RAUCH, Helene C. & PICKETT, M. J. ***Bordetella bronchiseptica* Bacteriophage.** *Canadian J. Microbiol.* Ottawa. 1961, Apr., v. 7, No. 2, 125–33, 4 figs. on 2 pls. [18 refs.]

38 phages were released spontaneously by 48 strains of *Bordetella bronchiseptica* from various sources, and 3 virulent mutants were also isolated. No further phages were obtained by exposing the bacterial strains to UV irradiation. All the strains were tested for sensitivity to the 41 phages: 13 were found to be completely resistant to all the phages, but each of the remaining 35 strains had a unique phage sensitivity pattern.

Phages isolated from *B. bronchiseptica* grew on *B. parapertussis*, providing further evidence of the close taxonomic relationship of the 2 species. The phages did not grow on *B. pertussis* or on *Bacterium alkaligenes*.

Janice Taverne

GHOSH, S. N. & MUKERJEE, S. **Neutralization of Cholera Bacteriophages by Extracts of *Vibrio cholerae*.** *Ann. Biochem. & Exper. Med.* Calcutta. 1960, Sept., v. 20, No. 9, 251–6. [13 refs.]

[An abstract of this paper appeared in the *Tropical Diseases Bulletin*, 1961, v. 58, 1010.]

VIRUSES

The order in this section is:—**General; Psittacosis-Lymphogranuloma group; Pox group; Respiratory group; Reovirus group; Enteric group; Arthropod-borne group; Others.**

BULL. SCHWEIZ. AKAD. MED. WISS. 1960, Oct., v. 16, No. 3, 131–205, 5 figs. [Numerous refs.] Virologisches Symposium, Bern, 17. 10. 1959. **[Virological Symposium, Berne, 17th October, 1959]**

The proceedings of a virological symposium held in Berne in October 1959 by the Swiss Academy of Medical Sciences are published in the form of 5 papers which are mostly devoted to descriptions of work on virus mutation.

In the first paper (*Introduction to General Virology*, pp. 131–140), C. HALLAUER reviews the properties of viruses, which inevitably stamp them as non-living infectious matter, and then points out that the main characteristic of viruses is their ability to integrate their genetic material with the genome of the host cell. They thus resemble transforming factors, but also possess a mechanism of transmission which enables them to enter the cell.

J. M. HOSKINS (*Host-Controlled Variation in Animal Viruses*, pp. 141–154) reviews the literature on the changes which can be produced in a virus by passage through the animal host, beginning with the O–D variation of influenza virus, and passing to the changes which may occur in attenuated strains of poliomyelitis virus. The author then describes experiments carried out by him with encephalomyocarditis virus in order to demonstrate the occurrence of host-controlled variation. The virus grown in mouse brain is normally incapable of multiplying in monolayer cultures of sarcoma 180 cells, but a variant could be isolated which grew in the cultures and caused cell destruction. After passage through mouse brain, however, the ability to grow in sarcoma 180 cells was lost, and it could be shown that this change was not due to the presence of an inhibitor in mouse brain, but that a modification in the properties of the virus had arisen during a single cycle of multiplication in mouse brain. The ability to grow in sarcoma 180 cells was restored after a single passage in Krebs-2 ascites cells.

K. W. MUNDRY (*The Production of Virus Mutations with a Plant Virus as Model*, pp. 155–170) describes the effect of nitrous acid in producing mutations in tobacco mosaic virus. The amino groups of the virus ribonucleic acid are thereby transformed into hydroxyl groups, so that adenine is transformed into hypoxanthine, guanine into xanthine and cytosine into uracil without any disruption of the general structure of the molecule. The infectivity of the ribonucleic acid is thereby largely destroyed, but the type of infection which still results shows differences from that produced by the initial virus, and a mutation has evidently been brought about by chemical means. A study of the kinetics of the process reveals that the oxidative deamination of only 1 of the 6,000 bases present in the ribonucleic acid molecule is sufficient to produce a mutation.

In the following paper C. HALLAUER (*Variants and Mutants in Viruses Pathogenic for Animals*, pp. 173–184) describes the production of avirulent variants by prolonged passage in cultures of human tissues. Fowl plague and Newcastle disease viruses maintained in this way lost their pathogenicity for the natural host but retained high immunizing potency. In the same way the pantropic Asibi strain of yellow fever virus could be attenuated until it was no longer pathogenic for rhesus monkeys.

The symposium is concluded with a paper by J. TOMCSIK (*New Trends in the Serological Diagnosis of Infectious Mononucleosis*, pp. 185–205). After a review of the literature, in which the effect of enzyme treatment upon the red cells used in heteroagglutination tests is discussed, the author proposes a method of his own. Bovine red cells are preferable, since they do not contain Forssman antigen, and their M-antigen is not destroyed by treatment with proteolytic enzymes. The red cells are treated with trypsin and the sera to be investigated are absorbed with guineapig kidney and tested in 5 serial 2-fold dilutions ranging from 1:12 to 1:192. In an examination of sera from 30 patients with infectious mononucleosis carried out by this method 28 gave titres of 48–192, whereas 119 of 127 sera from persons not suffering from infectious mononucleosis gave titres of 12 or lower. *D. J. Bauer*

GÉVAUDAN, P., RAY, R. & ARNAUD, G. Utilisation d'un milieu à base de protéose-peptone (No. 3 de Difco) pour la culture et l'entretien des souches cellulaires HeLa et KB. **[A Medium containing Proteose-Peptone (Difco No. 3) for Culture and Maintenance of HeLa and KB Cell Strains]** *Ann. Inst. Pasteur.* 1961, June, v. 100, No. 6, 821–4. [10 refs.]

CRANDELL, R. A., HERMAN, Y. F., GANAWAY, J. R. & NIEMANN, W. H. **Susceptibility of Primary Cultures of Feline Renal Cells to Selected Viruses.** *Proc. Soc. Exper. Biol. & Med.* 1961, Mar., v. 106, No. 3, 542–5, 6 figs.

The susceptibility of primary feline kidney cells to 24 viruses is reported. These viruses fell into 3 groups. 1. Those multiplying and producing cytopathic effects [CPE]: vesicular stomatitis, equine abortion, infectious bovine rhinotracheitis, ECHO 10, vaccinia, herpes, parainfluenza type 1 (Sendai) and adenovirus 4. 2. Those producing CPE but not multiplying indefinitely: parainfluenza type 3, canine hepatitis, adenovirus types 3 and 7 and Coxsackie B 1 to 5. 3. Those neither multiplying nor producing CPE: Newcastle disease, poliovirus types 1 to 3, Coxsackie A 9 and ECHO 4.

A. J. Beale

SCHMITTDIEL, E. Versuche zur Konservierung des Psittakose-Virus durch die Vakuumgefriertrocknung. [**The Preservation of Psittacosis Virus by Vacuum-Freeze-Drying**] *Zent. f. Bakt.* I. Abt. Orig. 1961, v. 181, No. 4, 446–50, 1 fig. [11 refs.]

The author finds 7·5% dextrose in skimmed milk an excellent suspending fluid for psittacosis virus. Suspended in such a medium, freeze dried and stored at 4°C. the virus titre was still some 50% of the original at the end of 6 months, whereas the titre of a buffered saline suspension similarly treated would have dropped by two-thirds. If the suspension were deep frozen (–15°C.) and not dried, the superiority of the skimmed milk medium was even more apparent.

S. P. Bedson

SMITH, K. O. & SHARP, D. G. **Interaction of Virus with Cells in Tissue Culture. II. Adsorption and Elution with Vaccinia Virus and L Cells.** *Virology.* New York. 1961, Mar., v. 13, No. 3, 288–93, 4 figs. [13 refs.]

These experiments were done by counting vaccinia virus particles by electron microscopy. Both the WR strain of virus (adapted to growth in L-strain cells), and calf lymph virus (not so adapted), adsorbed to and eluted from L cells at the same rate. When the WR strain of virus was inactivated by heat before being added to cells, no major difference in adsorption and elution rate was noted. In experiments involving the counting of all available virus particles over a period of 4 hours, it was found that about 40% of the original virus particles disappeared.

"This virus cannot be found by procedures that reveal virus that has been released from the cells to which it has been only *briefly* adsorbed" and there was thus no trace of it. *Colin Kaplan*

SMITH, K. O., GALASSO, G. & SHARP, D. G., with the technical assistance of S. W. WILBURN. **Effect of Antiserum on Adsorption of Vaccinia Virus to Earle's L Cells.** *Proc. Soc. Exper. Biol. & Med.* 1961, Mar., v. 106, No. 3, 669–71, 1 fig.

Using the technique of direct counting by electron microscope already reported [see Smith and Sharp above] the authors showed "with singular directness" that treating vaccinia virus with specific antiserum inhibited the adsorption of virus particles to susceptible cells. *Colin Kaplan*

APPLEYARD, G. **An Immunizing Antigen from Rabbit-Pox and Vaccinia Viruses.** [Correspondence.] *Nature.* 1961, Apr. 29, v. 190, 465–6.

A filtered virus-free extract was prepared from cultures of *ERK* 1 cells, *L* cells, primary rabbit kidney and chick embryo cells and from chick embryo chorio-allantoic membranes, all of which were infected with rabbit pox virus. This extract, when incubated with hyperimmune rabbit pox antiserum, removed the neutralizing antibodies. When injected into rabbits an antibody was produced which neutralized pock formation in the chorio-allantoic membrane. Tissues and cells infected with vaccinia virus produced a similar substance. Details are given of some of the physical characters of the substance. [No attempt was made to test the immunity of the rabbits by scarification with vaccinia virus. See AMIES below.] *Colin Kaplan*

KÜHN, O. Pocken-Schutzimpfstoff (trocken), eine Hilfe für unsere Dauerimpfstellen. [**Smallpox Vaccine (Dried), an Aid for Permanent Vaccination Stations**] *Ztschr. f.d.g. Hyg. u. ihre Grenzgebiete.* Berlin. 1961, Jan., v. 7, No. 1, 66–73, 2 figs. [23 refs.]

The author has investigated the production and application of a freeze-dried smallpox vaccine. Crude calf lymph was mixed with 5 parts of 25% aqueous solution of egg white, or of 10% sucrose solution, with the addition of penicillin and streptomycin; the mixture was clarified by low-speed centrifugation, placed in 1 cc. ampoules in volumes of 0·2 cc. and freeze-dried. The final product was white and readily soluble, and was dissolved in a mixture of equal parts of glycerol and saline before use. Cultures carried out 4 days after drying showed that the product was free from bacteria. During drying the virus titre declined by 1·5 log unit, but remained stable thereafter during a storage period of 6 months. Dried vaccine stored at room temperature for up to 5 months gave a satisfactory take in 42 of 47 persons. The product should be of value for creating stocks of long-life vaccine in permanent vaccination centres. *D. J. Bauer*

AMIES, C. R. **Loss of Immunogenic Properties of Vaccinia Virus Inactivated by Formaldehyde.** *Canadian J. Microbiol.* Ottawa. 1961, Apr., v. 7, No. 2, 141–52, 2 figs. [12 refs.]

Partially purified suspensions of vaccinia virus were exposed to 0·006 M formaldehyde for 300 hours at 20°–24°C. to ensure that no infectious virus was detectable after neutralization of the formaldehyde by sodium bisulphite. Intradermal inoculation of rabbits was found a more sensitive indicator of small amounts of residual infectivity than inoculation of monkey kidney monolayers. However, monolayers were more sensitive for the titration of virus of unimpaired infectivity. When inactivated virus was used to immunize rabbits by 2 subcutaneous injections at 10–day intervals, no antibody was demonstrable by titration in the skins of normal rabbits in either the first serum samples (10 days after first injection) or the second (13 days after second injection). Titration in tissue culture, however, showed a small antibody response in some rabbits after the first injection and a fairly brisk response in all rabbits after the second injection. The degree of response was not related to the dose of antigen. When these apparently

immune animals were challenged by cutaneous scarification with a potent vaccinia virus suspension they all reacted to it like normal animals, *i.e.* showed no immunity.

The author stresses the importance of challenging immunized animals and not relying only on serum antibody levels as an indication of immunity.

Colin Kaplan

ADERCA, I. & IANCONESCU, M. **Investigations on Herpes Virus in Human Amniotic and Embryo Cell Cultures.** *Rumanian Med. Rev.* 1960, Oct.–Dec., v. 4, No. 4, 14–18.

This paper reports the isolation in human embryo cell cultures [kind unspecified] of herpes simplex virus from 13 patients. The virus was identified by serum neutralization tests. Characteristic cytopathic effects, which included the formation of giant cells and of intranuclear inclusions, were observed both in these and in human amnion cells. Their significance is discussed.

Janice Taverne

FISHER, Thelma N. & FISHER, E., Jr. **Host Cell Metabolic Alterations following Herpes Simplex Infection.** *Virology.* New York. 1961, Mar., v. 13, No. 3, 308–14, 4 figs.

Glucose labelled with ^{14}C was added to the culture medium of nasal epithelial cells (DMB) infected with the HF strain of herpes simplex virus, and 48 hours later its metabolic products were assayed and their ^{14}C content determined. Acetate and pyruvate recovered were not radioactive and the same amounts were found in infected and uninfected cells. Lactate, however, was labelled. More was present in infected than in uninfected cultures but its specific activity was the same, suggesting that lactate was derived from glucose by the same process in both cases. Cultures which had been grown in the presence of cortisone acetate before infection gave similar results, but cytopathic changes in them were delayed.

Infected cultures produced less CO_2 than uninfected ones, but when glucose labelled at the C1 atom was used, the specific activity of metabolic CO_2 was higher in infected cultures, and highest of all in infected cortisone-grown cultures. When glucose labelled at the C6 atom was used, CO_2 collected from all cultures had a low specific activity . It thus appeared that in infected systems pentose-shunt metabolism was stimulated, with labelled CO_2 appearing upon decarboxylation of glucose–1–^{14}C.

Janice Taverne

COLEMAN, Virginia & JAWETZ, E. **A Persistent Herpes Simplex Infection in Antibody-Free Cell Culture.** *Virology.* New York. 1961, Mar., v. 13, No. 3, 375–7, 1 fig.

When seeded with the Z strain of herpes simplex virus, cultures of Maben cells (derived from a lung adenocarcinoma) developed a persistent infection which yielded large amounts of virus. Whenever the medium was sampled over a period of 9 months it was found to contain from 10^4 to 10^7 pock-forming units (PFU) per ml. Cytopathic changes characteristic of herpes were not observed, but the cells did not grow in smooth sheets. They were rounded and granular and broke up rapidly in trypsin. The persistent infection was not "cured" by adding antiserum to the cultures for 3 weeks.

In other cases of persistent infection of cell cultures by herpes the infection depends upon the presence of antibody in the medium preventing the spread of virus except between adjacent cells [WHEELER and CANBY, this *Bulletin*, 1960, v. 35, 1142; GIL FERNANDEZ, *ibid.*, 510]. In this case the medium did not contain herpes antibody, but special conditions were required for persistent infection to be established. A ratio of 1 PFU to 10^4 cells appeared to be essential; with less virus infection failed, with more the cells rapidly degenerated. Furthermore, persistent infection was only set up when cultures were maintained at 31°C. If the temperature was raised to 34°C. the cells released virus and degenerated. The authors failed to persuade the Z strain of virus to set up the same relationship with HeLa cells or L cells, or the HF strain with Maben cells or L cells.

Janice Taverne

GREENBERG, A. D. & STEWART, R. B. **Effect of Hydrocortisone on Herpes Virus-Infected HeLa Cells.** *Proc. Soc. Exper. Biol. & Med.* 1961, Mar., v. 106, No. 3, 666–9. [10 refs.]

HeLa cells have been found to have a greater rate of glycolysis in the presence of hydrocortisone, and, whether or not the steroid was present, infection with herpes simplex virus increased their rate of glycolysis (FISHER and FISHER, *Proc. Soc. Exp. Biol. Med.*, 1959, v. 100, 780). It is reported here that the amount of hydrocortisone labelled with ^{14}C taken up by HeLa cells was not increased by infection with the HF strain of herpes, and that uptake during 40 hours was the same whether cultures were incubated at 37°C. or at 4°C. Infected HeLa cells used less glucose than normal cells, but this reduced uptake was not so marked when hydrocortisone was present. Hydrocortisone reduced the amount of glucose within both normal and infected cells, but did not significantly alter the amount removed from the culture medium.

Janice Taverne

NIVEN, Janet S. F., ARMSTRONG, J. A., ANDREWES, C. H., PEREIRA, H. G. & VALENTINE, R. C. **Subcutaneous "Growths" in Monkeys produced by a Poxvirus.** *J. Path. & Bact.* 1961, Jan., v. 81, No. 1, 1–14, 16 figs. on 9 pls. [22 refs.]

Rhesus and cynomolgus monkeys could be infected with a filterable agent derived from "subcutaneous tumours" occurring spontaneously in captive rhesus monkeys in West Africa. This paper describes the

histopathology and cytology of material from experimentally infected animals. Fluorescence microscopy of sections treated with acridine orange showed abnormal cytoplasmic inclusions with the fluorescence characteristic of deoxyribonucleic acid. Electron microscopy of thin sections of "tumours" showed cells containing dense particles of about 280 $m\mu$ diameter. The appearance was recognized as being similar to that associated with infection by members of the pox virus group. The virus, when examined by light and electron microscopy, was morphologically similar to vaccinia virus. There was no demonstrable immunological relationship with the two other pox viruses—vaccinia and contagious pustular dermatitis.

Colin Kaplan

SUTTON, R. N. P. & TYRRELL, D. A. J. **Some Observations on Interferon prepared in Tissue Cultures.** *Brit. J. Exper. Path.* 1961, Apr., v. 42, No. 2, 99–105. [17 refs.]

Interferon was prepared by infection of human adult thyroid, human amnion, rhesus monkey and calf kidney cells with living influenza A virus (Kunz strain). Preparations, which were active in the homologous cell type in inhibiting ECHO 11 or parainfluenza type 1 infections, were tested against one or other of these viruses in the other cell types and, in addition, in human fibroblasts, human embryo kidney and lung and cynomolgus monkey kidney cells. Human amnion interferon was only active in homologous cells. Human thyroid and calf kidney interferons were active in some heterologus cells, but rhesus monkey interferon was active in all types of cells. In addition to ECHO 11 and parainfluenza 1, rhesus monkey interferon was found to inhibit Coe virus [this *Bulletin*, 1960, v. 35, 1057] and 2 of the Salisbury strains of common cold virus (FEB and HGP) [*ibid*, 1960, v. 35, 616] but not SV 17, a simian adenovirus. It was found that 1 dose of interferon lasted for about 5 days. Interferon was not effective after only 1 to 6 hours contact with cells, whereas it was effective after 18 hours contact. Interferon prepared in medium 199 without serum could be concentrated 10–fold by freeze-drying provided 0·1% gelatin was present. The solution was dialysed against distilled water before being freeze-dried.

On the basis of these experiments the authors suggest (with appropriate reservations about the validity of transfer of results in cells to effects in organisms) that interferon for use against respiratory viruses in man should be made in rhesus monkey kidney cells. They also stress the need for care in the use of interferon in man in the present state of our ignorance about this substance.

A. J. Beale

KILBOURNE, E. D., SMART, K. Marilyn & POKORNY, Barbara A. **Inhibition by Cortisone of the Synthesis and Action of Interferon.** [Correspondence.] *Nature.* 1961, May 13, v. 190, 650–51.

Interferon can be detected in the allantoic cavity of eggs infected with the PR8 strain of influenza A by assay in chorio-allantoic membrane *in vitro*. The multiplication of influenza viruses in the egg is enhanced by cortisone and certain other steroids, and one of the authors has shown that this effect is produced by the inhibition of virus interference [this *Bulletin*, 1958, 33, 405]. In the present experiments the authors show that interferon cannot be detected in eggs producing influenza virus in the presence of cortisone and that the effect of interferon on chick embryo cells can be prevented by treating them with cortisone.

D. A. J. Tyrrell

EATON, M. D. & SCALA, A. R. **Inhibitory Effect of Glutamine and Ammonia on Replication of Influenza Virus in Ascites Tumor Cells.** *Virology.* New York. 1961, Mar., v. 13, No. 3, 300–307.

Influenza multiplies partially in Krebs 2 ascites tumor cells, producing haemagglutinins (HA). The yield of HA in a medium containing glutamine and either bicarbonate or phosphate was reduced compared with that in a medium containing glutamate and phosphate or glucose and phosphate with and without bicarbonate. Investigating this the authors found that the cells produced ammonia in the presence of glutamine, and that 1·3 to 2·6 μgm% ammonia inhibited virus production. This inhibition was slightly enhanced by bicarbonate. To be effective glutamine or ammonia had to be added at the same time as, or before, the virus. [Full details are given in the original paper.]

D. A. J. Tyrrell

JERUSHALMY, Zohara, KOHN, A. & DE VRIES, A. **Interaction of Myxoviruses with Human Blood Platelets *in vitro*.** *Proc. Soc. Exper. Biol. & Med.* 1961, Mar., v. 106, No. 3, 462–6, 2 figs. [20 refs.]

A comparison was made between the adsorption-elution of myxoviruses from blood platelets and from red blood cells. The rate of adsorption of Newcastle disease virus (NDV) and influenza A (FM 1 strain) to platelets at 4°, 23° and 37°C. resembled the rate for red cells. Adsorption of influenza virus to platelets was maximal at 4°C., and of NDV at 37°C. Adsorption of influenza virus to red cells ceased at a concentration of 0·01 M or less NaCl but virus was still adsorbed to platelets at 0·0025 M NaCl. Less virus was eluted from platelets than from red cells and the process took a longer time. After a single cycle of adsorption-elution and also after treatment with receptor-destroying enzyme (RDE) platelets still adsorbed small quantities of the same virus. Treatment of platelets and red cells with RDE reduced the electrophoretic mobility of both almost to the same extent. The authors suggest that the incomplete elution of virus from platelets may be explained by assuming that virus is incorporated by the platelets and that, in fact, receptors for myxoviruses on red blood cells and platelets may be identical.

D. Taylor-Robinson

LIPPELT, H.; MANNWEILER, E. Das Verhalten von Influenzaviren in Gewebekulturen von Hühnerembryo-Nieren. I. Virusadsorption [**The Behaviour of Influenza Viruses in Chick Embryo Kidney Tissue Cultures. I. Virus Adsorption**] LIPPELT & MANNWEILER]. *Arch. f.d. gesamte Virusforschung.* 1961, v. 10, No. 5, 636–46, 4 figs. [19 refs.] II. Virusvermehrung [**II. Virus Multiplication**] [MANNWEILER]. *Ibid.*, 647–60, 7 figs. [32 refs.] III. Passage prototyper Influenzastämme, cytopathogene Wirkung von A/Singapur/1/57 und vergleichende ID_{50}-Titrationen [**III. The Passage of Prototype Strains of Influenza Virus, the Cytopathic Effect of A/Singapore/1/57 and Comparative ID50 Titrations**] [MANNWEILER]. *Ibid.*, 661–71, 6 figs. [26 refs.]

(1) In experiments concerning the adsorption of the A/Singapore/1/57 strain of influenza virus on chick embryo kidney monolayer cultures it was found that the proportion of virus taken up by the cells was independent of the multiplicity over a 1000-fold range, and amounted to about 80%. No uptake of virus could be observed with multiplicities lower than 1, and this was ascribed to the presence of inhibitors; when monolayer cultures were resuspended by trypsinization, washed 5 times and treated with virus as a cell suspension, adsorption of virus could be observed with multiplicities as low as 0·01.

(2) The yield of haemagglutinin after 24 hours from chick embryo kidney monolayers infected with the A/Singapore/1/57 strain of influenza virus was directly dependent upon the dose of virus used for infection, and attained a maximum with multiplicities above 1, whereas 72 hours after infection the yield was essentially the same with multiplicities ranging from 0·0001 to 100. The effect of variations in multiplicity on the production of non-infectious virus, yield per cell and the length of the eclipse phase were also studied.

(3) Cultures of chick embryo kidney cells gave satisfactory multiplication of the swine, PR8, FM1, A/Singapore/1/57, Lee and Sendai strains of influenza virus, but the 1233 strain of type C virus did not grow sufficiently well to be maintainable in passage. The cytopathic effect produced by the Asian strain is described. In tissue culture the strains gave titres about 2 log units lower than those obtained in eggs by allantoic inoculation. *D. J. Bauer*

OSATO, T. & ISHIDA, N. **The Labelling of Influenza Virus with Radioactive Phosphorus in Maitland Type Tissue Culture. First Report. Growth Characteristics of Myxoviruses in Tissue Culture.** *Tohoku J. Exper. Med.* 1960, Nov. 25, v. 72, No. 4, 322–7. [15 refs.]

^{32}P-labelled influenza A virus was prepared by incubating 5 chorioallantoic membranes from 15-day-old eggs with phosphorus-free Hanks solution containing ^{32}P and virus (allantoic fluid) at 37°C. for 24 hours. The supernatant fluid, after centrifugation, was put through 2 cycles of adsorption to and elution from chicken red cells. The second eluate was ultracentrifuged for 1 hour, the sediment resuspended in phosphate-buffered saline and then dialysed against this buffered saline at 4°C. The supernatant after a slow-speed centrifugation was the labelled virus. ^{32}P in a concentration of 200 μc per membrane produced an activity of 8·22 counts per minute per haemagglutinin unit. Such a preparation contained about 5% non-virus ^{32}P. This is a preliminary study to further work on the growth characteristics of myxoviruses [this *Bulletin*, 1961, v. 36, 813]. *D. Taylor-Robinson*

BLASKOVIC, D., MAKSIMOVIC, N. A., STYK, B. & ALBRECHT, P., with the technical assistance of R. ULBRÍKOVÁ & J. RAUS. Priebeh adaptácie inhibítor-rezistentného vírusu chrípky A2 na fretku. [**Course of Adaptation of the Inhibitor-Resistant Influenza Virus A2 to Ferrets**] *Československ. Epidemiol., Mikrobiol., Imunol.* Prague. 1961, v. 10, No. 3, 158–65, 4 figs. on 2 pls. [11 refs.]

The English summary appended to the paper is as follows:—

"1. The tenth egg passage of the inhibitor-resistent strain of the influenza virus A2/Bratislava 4/57 was pathogenic for ferrets. The degree of pathogenicity was studied by investigating the adaptation process of the virus to the animal in 26 passages in ferrets.

"2. The adaptation process was evaluated from changes of the properties of the virus with regard to the macroorganism and the reaction with specific antibodies and non-specific inhibitors.

"48 hours after infection only in the histological appearance of the trachea and lower respiratory tract in the 1st to 8th passage signs developed which suggested that the virus invaded sensitive cells, and caused the formation of basophil inclusions and dystrophic changes. From the 5th passage onwards it caused a marked proliferation of the epithelium in small bronchi. In the pulmonary parenchyma a swelling of the alveolar cells and infiltration of the septa developed.

"In the higher passages [9th–17th] 3 days after infection degenerative processes disappeared from the trachea and the changes in the bronchi and the pulmonary parenchyma became more marked. Pneumonic changes developed when there was a large number of viruses in the inoculum [10^9/ml.], the virus was, however, already adapted. The amount of the administered virus in the inoculum plays an important role as far as the type and extent of pathological changes in the infected animal is concerned.

"3. Strains adapted to ferrets are more avid and sensitive to specific antibodies as well as to non-specific inhibitors.

"4. An infection during the period of a well developed antibody response 6 weeks after infection did not lead to an enhanced skin sensitivity to homologous or heterologous strains of Group A and their internal S- or g-antigen."

HOMMA, M., KUDO, H. & ISHIDA, N. **Studies on Experimental Influenza in Mice. IV. Growth Characteristics of the PR8 Virus in Mouse Tissues explanted *in vitro*.** *Tohoku J. Exper. Med.* 1960, Nov. 25, v. 72, No. 4, 338–47, 5 figs.

The growth of influenza A (PR8) virus in mouse tissue was studied in 3 types of culture. Maitland-type cultures of brain, lung, liver, kidney, spleen, pancreas and muscle from adult white mice did not support growth. Further, on Zinsser's agar slant cultures the same tissues, except lung tissue, did not support growth of virus. However, the final infective titre was almost one-tenth of that obtained in chick embryos. Roller tube cultures (with explants) of the tissues were more successful; growth of virus was demonstrated in lung, liver and kidney. *D. Taylor-Robinson*

KLAMERTH, O. Die Beeinflussung der Aktivitäten von Gewebsenzymen durch Virusinfektion. [**The Influence of Virus Infection on the Activity of Tissue Enzymes**] *Arch. f.d. gesamte Virusforschung.* 1961, v. 10, No. 5, 578–87, 4 figs. [29 refs.]

An investigation has been made of the activity of a number of enzymes in the chorioallantoic membrane during the course of multiplication of the Crawley strain of type B influenza virus. Fertile eggs at the 13th day of incubation were infected in the allantoic cavity with a dose of virus calculated to give a multiplicity of 3–4, and at intervals up to 25 hours the chorioallantoic membranes were removed from groups of 10 eggs, homogenized in 10 volumes of 0·25 M sucrose and used for enzyme determinations. A decline in rhodanase activity was noted during the course of infection, and a slight rise in alanine transaminase and adenosine monophosphate deaminase activities. *D. J. Bauer*

ABINANTI, F. R., CHANOCK, R. M., COOK, M. K., WONG, D. & WARFIELD, M. **Relationship of Human and Bovine Strains of Myxovirus Para-Influenza 3.** *Proc. Soc. Exper. Biol. & Med.* 1961, Mar., v. 106, No. 3, 466–9. [18 refs.]

ABINANTI and HUEBNER [this *Bulletin*, 1960, v. 35, 90] reported no differences in antibody responses to HA–1 (human) and SF–4 (bovine) strains with human, bovine, rabbit or rooster sera. HAMPARIAN and HILLEMAN (in press), however, distinguished between the viruses and showed that guineapigs developed a specific response after infection but that the specificity was lost after repeated exposure to the same virus. This explained the discrepancy between the 2 studies. The present report confirms the distinction between the 2 viruses.

Guineapigs were inoculated intranasally with virus and bled 14 days later when they were also given soluble antigen intraperitoneally and then bled out after 8 days. Haemagglutination-inhibition (HI) and neutralizing antibody to the homologous strain of virus frequently appeared earlier and was 4-fold or more greater than antibody to the heterologous strain. Neutralizing antibody in children after a natural infection with HA–1 virus showed a similar 4-fold rise and one child after re-infection developed a low level of antibody to the bovine strain. Further, sera from dairy calves infected in nature showed greater homologous than heterologous HI antibody levels. Finally, each of 23 human and 7 bovine strains originating from various states and countries and isolated in different years resembled its respective prototype but the human isolates were inhibited in HI tests by HA–1 antiserum at a 4–fold or higher titre than with SF–4 antiserum, and *vice versa* with bovine isolates. *D. Taylor-Robinson*

GRANOFF, A. **Induction of Newcastle Disease Virus Mutants with Nitrous Acid.** *Virology.* New York. 1961, Apr., v. 13, No. 4, 402–8, 3 figs. [16 refs.]

"*In vitro* treatment of Newcastle disease virus with nitrous acid inactivated the virus exponentially and, at the same time, produced a variety of small-plaque-type mutants. Mixed infection of chick embryo monolayers with a number of the induced mutants in pairwise crosses yielded no recombinant wild-type plaques."

GRANOFF, A. **Studies on Mixed Infection with Newcastle Disease Virus. III. Activation of Non-plaque-Forming Virus by Plaque-Forming Virus.** *Virology.* New York. 1961, May, v. 14, No. 1, 143–4.

BONTSCHEFF, N. Ätiologische Forschungen der Virus-Pneumonie bei den Ferkeln. [**Research concerning the Aetiology of Virus Pneumonia in Pigs**] *Zent. f. Bakt.* I. Abt. Orig. 1961, v. 181, No. 4, 417–22. [14 refs.]

——. Kultivierung des Ferkelpneumonie-Virus in Hühnerembryonen und Erforschung seiner Eigenschaften. [**Cultivation of a Virus causing Pneumonia in Pigs by means of Chicken Embryos and Research concerning its Properties**] *Ibid.*, 423–8.

MOGABGAB, W. J. & HOLMES, Barbara. **2060 and JH Viruses in Secondary Monkey Kidney Cultures.** *J. Infect. Dis.* 1961, Jan.–Feb., v. 108, No. 1, 59–62, 2 figs.

The viruses [also called ECHO 28] were titrated in stationary primary or secondary monkey kidney cell cultures. The latter could apparently be infected by 15 to 30 times less virus than the former and the sensitivity of rolled primary cultures was greater than stationary cultures. When neutralization tests were done in secondary monkey kidney cultures the results were easier to read because of the more marked cytopathic effect. A $10^{2 \cdot 3}$–fold change in the concentration of virus used in the test produced a 10–fold change in the neutralization titre. *D. A. J. Tyrrell*

PELON, W. **Classification of the "2060" Virus as ECHO 28 and Further Study of its Properties.** *Amer. J. Hyg.* 1961, Jan., v. 73, No. 1, 36–54, 4 figs. [22 refs.]

2060 and JH viruses (PELON *et al.*, *Bact. Proc.*, 1956, 67; PRICE, *Proc. Nat. Acad. Sci.*, 1956, v. 42, 893) have been shown to be serologically identical and both agents have been accepted as ECHO 28 (2060 virus being the prototype). The virus is unrelated to other members of the enterovirus family, is not sensitive to ether, has a particle size of approximately 16 mμ measured by filtration and by using BLACK'S formula (*Virology*, 1958, v. 5, 391), and antibodies to it are present in pools of human sera. The virus is also non-pathogenic for suckling mice and for monkeys inoculated intracerebrally. This virus has proved rather difficult to work with but many of the difficulties have now been overcome by improvements in the method of culture. It was found, by using monkey kidney cells, that the titre and the cytopathic effect of the virus were maximal when the concentration of sodium bicarbonate did not exceed 0·084%. When the level reached 0·12% there was a marked decline in virus titre. It was also found that residual serum inhibited the virus, reducing the titres as much as 10-fold. It was necessary to wash the cultures thoroughly to remove the residual serum used for cell outgrowth and to employ a serum-free medium during the virus growth phase. Horse, rabbit, monkey and calf serum batches that were tried were all inhibitory.

HOLPER and MARQUIS (*Bact. Proc.*, 1959, 63) reported that the titre of ECHO 28 was higher in young than in older cultures but this observation could not be confirmed. In fact the titres were, if anything, slightly higher in 11-day-old than in 6-day-old cultures.

The cytopathic effect produced by the virus is illustrated and looks remarkably similar to that produced by other enteroviruses and by the Salisbury strains of common cold virus. The changes are first seen as scattered foci of rounded refractile cells of various sizes, occurring especially at the margin of the cell sheet. The cells fall off the glass and gradually the area of healthy cell sheet is reduced. It is important not to handle the cells roughly as they may all be detached leaving perfectly normal cells on the glass although the size of the cell sheet is reduced. It is suggested in studying this virus that the area of the cell sheet be marked at the time of virus infection so that the loss of cells can be followed.

It was found that the virus could be concentrated in an ultracentrifuge, in 0·06% gelatin at 78,000 G for 3 hours. The virus appears not to be very stable at 36°C. Attempts to prepare a satisfactory complement-fixing antigen were unsuccessful as also were attempts to produce plaques on monkey kidney cells. It was not possible therefore to purify the prototype virus by selecting a single plaque but instead purification was achieved by a terminal dilution technique in tubes. *A. J. Beale*

EGGERS, H. J. & TAMM, I. **2-(α-Hydroxybenzyl)-Benzimidazole (HBB) as an Aid in Virus Classification.** *Virology.* New York. 1961, Apr., v. 13, No. 4, 545–6, 1 fig.

Eggers and Tamm have shown that ECHO 28, ECHO 10, 22 and 23 and the HGP strain of common cold virus differ from other enteroviruses in being insusceptible to the inhibitory effect of 2-(α-hydroxybenzyl) benzimidazole. ECHO 10 is now classified as a reovirus [SABIN, this *Bulletin*, 1960, v. 35, 514]. ECHO 22 and 23 have been shown to produce distinctive cytopathic effects [SHAVER *et al.*, below]. It may well be therefore that ECHO 28 virus will also prove to be miscast in the Enterovirus family.

A. J. Beale

SHAVER, Dorothy N., BARRON, A. L. & KARZON, D. T. **Distinctive Cytopathology of ECHO Viruses Types 22 and 23.** *Proc. Soc. Exper. Biol. & Med.* 1961, Mar., v. 106, No. 3, 648–52, 3 figs. [11 refs.]

In a survey of the cytopathic effects of enteroviruses it was found that among the first 24 ECHO types, 3 produced distinctive cytology. The first was ECHO 10 which has now been removed from the ECHO into the reovirus group [SABIN, this *Bulletin*, 1960, v. 35, 514]. These changes have been described by DROUHET [*ibid.*, 1959, v. 34, 400]. The cytological changes produced by ECHO 22 and 23 are closely similar and those for type 22 are fully described in this paper. The changes are listed in order of appearance.

1. Rounding of cells and appearance of an eosinophilic cytoplasmic mass with no nuclear changes.
2. Decrease in staining intensity of the nucleolus.
3. Disappearance of nucleolus without changes in chromatin.
4. Beading of nuclear chromatin either diffusely or peripherally.
5. Disappearance of chromatin leaving an "empty" appearing nucleus.

On staining with acridine orange and viewing with ultraviolet light greenish-staining cytoplasmic masses may be seen, and thickened green-staining (DNA-containing) nuclear membranes.

The value of examination of stained preparation of infected cells both for the rapid identification and also for the classification of viruses is stressed. *A. J. Beale*

BHAGWAT, S. M. & GHARPURE, P. V. **The Enteroviruses.** *J. of J.J. Group Hosps. & Grant Med. College.* Bombay. 1961, Jan., v. 6, No. 1, 27–36. [12 refs.]

A brief, rather superficial, review of work on enteroviruses especially in India is presented, together with the incidence of enteroviruses in the Bombay area. The following enteroviruses have been discovered in India; poliovirus types 1, 2 and 3, Coxsackie A 1, 3, 4, 9, 10, 12 and 14, Coxsackie B 1, 3, 4, and 5 and ECHO 1, 3, 5, 7, 11 and 13. Figures for the incidence of enteroviruses in faecal samples [from children of various age-groups but of unspecified clinical state] during 1955 to 1959 are presented. 5% of the specimens showed an enterovirus but the incidence varied, being highest in young children and between July and October. In those aged 1 to 2 years the rate approaches 50% for these months. Polio-

viruses, often attenuated, have been isolated from a "good number" of faecal samples from healthy children.

A. J. Beale

LUND, Ebba. **Influence of Age and Cell Number of a Tissue Culture on its Susceptibility to Poliovirus.** *Arch. f.d. gesamte Virusforschung.* 1961, v. 11, No. 1, 111–19, 4 figs. [11 refs.]

In this paper the influence of the age and number of cells in a tissue culture on the titre of all 3 types of poliovirus was investigated by using HeLa and Detroit–6 cells. It was found that the titre was significantly higher in young than in older cultures. Cultures used on day 1 not only gave higher titres but were destroyed more rapidly by poliovirus. The titres were also found to be higher if the cultures were used immediately after fluid change than if they were left for 1 to 4 days before inoculation with virus. Finally, it was found that the number of cells in a culture influenced the titre obtained. The highest titres were obtained by using 50,000 cells in a culture, and titres were successively lower with lesser numbers of cells. It is conjectured that one of the reasons for the lower sensitivity of older cultures is the more rapid reduction of the *p*H of the nutrient medium to regions which are inhibitory on virus production.

A. J. Beale

LUND, Ebba & LYCKE, E. **The Effect of Oxidation and Reduction on the Infectivity of Poliomyelitis Virus.** *Arch. f.d. gesamte Virusforschung.* 1961, v. 11, No. 1, 100–110, 7 figs. [22 refs.]

The effect of alterations in the oxidation-reduction potential on the inactivation of type 3 poliovirus at 37°C. was investigated. It was found that at oxidation-reduction potentials of −250 to +200 millivolts the rate of virus inactivation was the same as in phosphate buffer. The inactivation rate was enhanced at potentials above 300 millivolts. At potentials of 400 or 500 millivolts the rate of inactivation was extremely rapid but was no longer linear, decreasing with continued incubation at 37°C. The oxidizing agent used was potassium permanganate. If the potential was reduced to a normal level with sodium sulphide then the inactivation was stopped. The rate of inactivation did not differ in the presence of atmospheric oxygen or in the presence of nitrogen for a constant oxidation-reduction potential. It is noted that the deviation from a linear inactivation rate is somewhat similar to that described for the inactivation of poliovirus with formaldehyde.

A. J. Beale

JUNGEBLUT, C. W., KODZA, Helen & FURUSAWA, E. **Cytopathogenic Propagation of Poliomyelitis Virus in Normal and Leukemic Guinea Pig Spleen Cell Cultures.** *Arch. f.d. gesamte Virusforschung.* 1961, v. 11, No. 1, 176–81, 2 figs. [11 refs.]

The authors describe the establishment of a number of cell strains derived from normal or leukemic tissues of the guineapig. These were maintained in medium 199 with 10% horse serum and 5% human serum. After 4 or 5 passages these cell lines, unlike the primary guineapig cells, were found to be susceptible to all 3 types of poliovirus. Concurrently with the establishment of susceptibility to poliovirus, the cell strains were found to produce antisera in rabbits with a lower titre of antibodies against normal or leukemic guineapig spleen extracts and against Forssman antigen. It is thought that the loss of species-specific antigens may be related to the acquisition of susceptibility to poliovirus.

[It seems probable in view of the findings of COOMBS *et al.* (*Nature*, 1961, v. 189, 503) that the ERK line of embryo rabbit kidney cells which were found to be susceptible to poliovirus are in reality human in origin. So far as the abstracter is aware there is no evidence that a cell of non-primate origin has definitely been established as susceptible to poliovirus. The authors do not make it clear in this paper if they were maintaining HeLa cells in their laboratory but, since the poliovirus pools that were used were grown in HeLa cells, it seems that this is possible and, if so, the possibility of contamination of guineapig cultures with these cells must remain.]

A. J. Beale

TAYLOR, Joyce & GRAHAM, A. F. **Analysis of a Plaque Assay Method for Purified Poliovirus MEF-1.** *Virology.* New York. 1961, Apr., v. 13, No. 4, 427–38, 6 figs. [16 refs.]

MEF–1 type 2 poliovirus purified by adsorption and elution from a Dowex–1 resin column was found, in the electron microscope, to have 48 physical particles to every infectious particle determined by plaque assay on monkey kidney cells. It was found that the routine plaque assay detected only approximately 60% of the infectious particles and that all cells are susceptible to infection by 1 particle of MEF–1 virus. The reason for the ratio of 1/30 (reduced from 48 by allowing for assay insusceptibility) was undetermined. There may be only 1 particle in every 30 capable of initiating infection or there may be many sites on the cell which allow adsorption, but do not allow virus to enter the cell.

A. J. Beale

JOKLIK, W. K. & DARNELL, J. E., Jr. **The Adsorption and Early Fate of Purified Poliovirus in HeLa Cells.** *Virology.* New York. 1961, Apr., v. 13, No. 4, 439–47, 3 figs. [13 refs.]

The authors of this paper deal with much the same topic as TAYLOR and GRAHAM [above] and use the same general technique of following the adsorption of radioactive purified poliovirus (the Mahoney strain of type 1) both by following the radioactive label and assaying infectivity. They found that virtually all virus particles were adsorbed to the cells, but thereafter the fate of particles varied. 50–60% of the adsorbed virus was eluted. This eluted virus still contained its full complement of infectious RNA but did not adsorb to

cells and was virtually non-infectious (titre 10^4-fold lower). The virus rapidly broke down in caesium chloride, but sedimented like normal poliovirus in a sucrose density gradient. Virus eluted at 37°C. from cells so that 50% of the adsorbed virus was released in 20 minutes; elution did not occur at 0°C. A small fraction of adsorbed virus persisted for 6½ hours. The remainder of the virus was degraded to a state sensitive to RNAase. Only a small fraction of adsorbed virus initiated infection. The authors favour the idea that all virus particles can be adsorbed and produce infection, chance alone determining which particles actually initiate infection. *A. J. Beale*

EGGERS, H. J. & SABIN, A. B. **A Phase Contrast Microprecipitin Test with Poliovirus Antigens. I. Properties of the Antigens and Antibodies and Optimum Conditions for Reaction.** *Arch. f.d. gesamte Virusforschung.* 1961, v. 11, No. 1, 120–51, 6 figs. [24 refs.] **II. Occurrence and Development of Microprecipitin Antibody after Natural Inapparent Infections, after Inoculation of Salk Vaccine, after feeding of Attenuated Live Poliovirus Vaccine, and in Disease caused by Polioviruses and other Enteroviruses.** *Ibid.*, 152–75. [19 refs.]

(i) A microprecipitin test for poliovirus antigens is described. The volume of reagents was reduced to 0·01 ml. and the results were read by phase contrast microscopy after 4 hours incubation at 36°C. The development of the technique is described in detail. Virus antigens, even of high infectivity titre ($10^{8\cdot5-8\cdot8}$ TCD50 per ml.), required concentration before satisfactory precipitin was obtained. It was found, however, that when the antigens were concentrated 50-fold by centrifugation there was a much greater concentration of precipitating antigen than expected. This discrepancy was not due to the presence of an inhibitor in the tissue culture fluid since the precipitin titre was the same whether the deposit was resuspended in supernatant fluid of saline. The authors suggest that the effect may have been due to alteration of the physical state of the virus particles by centrifugation. Cross reactions between types were noted. Thus, type 2 antigen reacted with type 1 and 3 antisera and type 1 antigen with type 2 antisera, but these cross reactions were of low titre. Attenuated strains of poliovirus produced satisfactory antigens which were slightly less potent than those from virulent strains. Early tests were done with hyperimmunized rabbit sera but, unexpectedly, monkey antisera gave no reaction in the precipitin test. Human sera, on the other hand, did give precipitation. Serum titres were found to be slightly higher if unheated sera were used and antigen–antiserum mixtures were held for 18 hours at 4°C. after incubation at 36°C. Purified D antigen of Mahoney virus gave similar results to the crude tissue culture concentrates.

(ii) The test was used to investigate the poliomyelitis precipitating antibody titre of healthy individuals after vaccination with killed and attenuated poliovaccine and after clinical disease. It was found that some sera showed the appearance of Coxsackie A9 precipitating antibodies during poliovirus infection. However, no example of a rise in poliovirus precipitins was observed in paired sera from patients infected with other enteroviruses. It was found that precipitins developed more slowly and disappeared more quickly than neutralizing antibodies and that there was no correlation between these two sorts of antibodies. The method has considerable limitations as a diagnostic tool but the authors suggest that a titre of 1/4 by their technique might be taken as evidence of recent poliovirus infection.

[The results obtained are at variance with those obtained by many authors (*e.g.* LE BOUVIER, this *Bulletin*, 1958, v. 33, 412; 1960, v. 35, 316, 405) using the gel diffusion technique. It is probable that reactions taking place in fluid media are confused owing to the presence of at least 2 poliovirus antigens (D and C) and also by the presence of other components of the culture medium. LE BOUVIER (*ibid.*, 1960, v. 35, 402), for example, has shown that horse serum decreases the heat stability of the D antigen of poliovirus.] *A. J. Beale*

SCHMIDT, W. A. K., HÖPKEN, W. & WOHLRAB, R. Untersuchungen zur Komplementbindungs-Reaktion der Poliomyelitis. I. Verwendung konzentrierter und fraktionierter Antigene. **[Investigations of the Complement-fixation Test in Poliomyelitis. I. The Use of Concentrated and Fractionated Antigens]** *Arch. f.d. gesamte Virusforschung.* 1961, v. 10, No. 5, 617–35, 1 fig. [37 refs.]

Types 1, 2 and 3 poliomyelitis virus growth in FL cells was purified by the method of SCHWERDT and SCHAFFER [this *Bulletin*, 1957, v. 32, 906], which involves precipitation with cold methanol at *p*H 4, extraction of the precipitate with *n*-butanol, repetition of the first step and ultracentrifugation. An overall virus enrichment factor of 500, 80 and 63 for the 3 respective types was achieved by the treatment, and the final products had complement-fixation titres of 1,600, 400 and 200. The type 1 final products could be separated into 2 fractions (C and D) by ultracentrifugation in a sucrose density gradient, one of which (D) possessed nearly all the infectivity and complement-fixing activity. The purified virus preparations and fractions C and D type 1 virus were used as complement-fixing antigens in the investigation of paired sera from 30 patients from whom type 1 virus had been isolated. Fraction D fixed complement in the same way as the purified virus, and its activity was still retained after heating at 56°C. for 30 minutes. *D. J. Bauer*

PONTECORVO, M. & PICCIOTTO, L. **Observations on the Relation between Content of Virus Antigens and Immunogenic Potency of Inactivated Poliomyelitis Vaccine.** *Riv. Istituto Sieroterap. Ital.* 1961, Jan.–Feb., v. 36, No. 1, 55–61, 3 figs. [10 refs.]

The results of antigenicity tests on Italian killed poliovaccine, expressed as the antigenic extinction titre

in guineapigs based on the method of GARD [MELEN *et al.*, this *Bulletin*, 1957, v. 32, 1115], are presented. The authors agree with GARD *et al.* [*ibid.*, 1959, v. 34, 587] that a titre of 10^{-2} is required for all 3 types if 100% antibody conversion in triple negative children is to be achieved. They find that this is regularly attained with type 2 (24 out of 26 batches). Type 3 is nearly as good with 18 out of 26 batches reaching this titre and type 1 much less good with only 11 out of 26 batches reaching an antigen extinction titre of 10^{-2}. The authors believe from their experience that, in order to achieve these potencies, starting titres for types 1, 2 and 3 should be $10^{7.7}$, $10^{7.0}$ and $10^{7.3}$ TCD50 per ml., respectively, although they note that because of the titration inaccuracies these estimates cannot be taken as final. *A. J. Beale*

NÚÑEZ-MONTIEL, O., VITELLI-FLORES, J. & WEIBEL, J. **Finding of Virus Particles in Cultivated Monkey Kidney Cells infected with Coxsackie Virus B5.** *Virology*. New York. 1961, May, v. 14, No. 1, 147–50, 8 figs. [10 refs.]

LEHMANN-GRUBE, F. & SYVERTON, J. T. **Pathogenicity for Suckling Mice of Coxsackie Viruses adapted to Human Amnion Cells.** *J. Exper. Med.* 1961, May 1, v. 113, No. 5, 811–29, 8 figs. [43 refs.]

It was found that 12 Coxsackie viruses (A 9–11, 13–15, 18 and B 1–5) could be adapted to human amnion cells and that on serial passage in these cells the titre increased for cells but decreased markedly for mice. It was found for most strains, however, that reversion to virulence for mice occurred rapidly on passage in mice. This return to mouse virulence was not associated with much loss of titre in human amnion cells. Coxsackie A 15, B 1, 2 and 5 reverted to virulence more slowly, as did the other viruses when the virus passaged in human amnion cells was purified by limit dilution, or where possible by picking single plaques. The dose response curve for Coxsackie viruses is normally steep in mice but after cell passage it becomes very flat, suggesting that the residual low mouse virulence is not due to a few fully virulent particles but to a lowering of the virulence of all particles. *A. J. Beale*

GRODUMS, E. Irene & DEMPSTER, G. **Encephalitis in Experimental Coxsackie B-3 Infection.** *Canadian J. Microbiol.* Ottawa. 1961, Apr., v. 7, No. 2, 175–84, 9 figs. (8 on 2 pls.) [17 refs.]

The authors are exhaustively studying the infection of mice with Coxsackie B 3 virus [GRODUMS and DEMPSTER, this *Bulletin*, 1960, v. 35, 517 *bis*.]. They find that the older the mice at the time of inoculation with B 3, the less the severity of the resulting encephalitis. This is not due mainly to barriers forming between peripherally inoculated virus and the brain during growth, since it is also observed after direct inoculation into the CNS. The pattern of damage in the brain was examined and the most striking observation was the great cerebral damage with sparing of the cerebellum, regardless of which of these two parts of the CNS received the inoculum. It was found, moreover, that virus multiplied to the same extent in both these sites. Also, in older mice, virus multiplied in the brain but caused no damage. There appeared (the cerebellum apart) to be a rough correlation between the commencement of myelination and the fall in susceptibility of the CNS to damage following Coxsackie B 3 virus infection. *A. J. Beale*

ROBBA, L. & VIRAT, J. Les réactions croisées dans la déviation du complément pour le diagnostic sérologique des affections à entérovirus avec les antigènes Coxsackie groupe B et ECHO. [**Complement-Fixing Cross Reactions between Coxsackie B and ECHO Antigens in the Diagnosis of Enterovirus Diseases**] *Ann. Inst. Pasteur.* 1961, Apr., v. 100, No. 4, 524–30. [21 refs.]

The authors have previously described a method of preparing complement-fixing antigens from enteroviruses grown in KB cells [ROBBA and VIRAT, this *Bulletin*, 1961, v. 36, 411]. They now describe the reactions obtained with these antigens both with immune sera made in animals and with sera from patients. The existence of cross reactions between enteroviruses is illustrated in a series of tables. *A. J. Beale*

HENDERSON, J. R. & TAYLOR, R. M. **Studies on Mechanisms of Arthropod-Borne Virus Interference in Tissue Culture.** *Virology*. New York. 1961, Apr., v. 13, No. 4, 477–84, 4 figs. [19 refs.]

Chick embryo monolayer cultures were infected with Mayaro virus (4th mouse passage twice plaque purified) at a multiplicity of 1, then washed and infected with Sindbis virus (5th mouse passage twice plaque purified) at a similar multiplicity. Sindbis was interfered with so that its titre after 1 growth cycle was only 1 log compared with 4 log when heated Mayaro or normal mouse brain which had no interfering effect were used as controls. A multiplicity of at least 0·1 of Mayaro was found necessary to cause detectable interference and the degree of interference increased almost exponentially with the time allowed for adsorption before Sindbis was added. Mayaro treated with RNase or 2% deoxycholate also interfered but virus treated with deoxycholate followed by RNase did not (the deoxycholate treated agent thus appears to be viral nucleic acid), nor did neutralized virus, heated virus or ultraviolet inactivated virus.

Suspensions of Mayaro-infected mouse brains and cultures were centrifuged at 35,000 r.p.m. for 3 hours. The suspended pellets and supernatants were compared for interfering effect. The mouse brain pellet interfered but not the culture pellet because of low multiplicity. The culture supernatant but not the mouse-brain supernatant also interfered. This inhibitor, not associated

with the infectivity, appeared in heavily infected cultures after about 72 hours' incubation and increased at least up to 96 hours. It was stable at 37°C. for at least 10 days and at refrigerator temperature for at least 20. It was not inactivated by a dose of ultraviolet sufficient to inactivate live virus.

In this system there thus appear to be 2 types of interference: that due to live virus and that due to inhibitor [? interferon]. *C. E. Gordon Smith*

MÁLKOVÁ, D. **Spread of Tick-Borne Encephalitis Virus in the Body of a Non-Susceptible Animal—Rabbit.** *Acta Virologica.* Prague. 1961, May, v. 5, No. 3, 137–40.

20 million mouse LD50 of 47th passage Hypr strain were inoculated into the hind leg of rabbits. 1, 2, 3, 6, 10 and 14 days later a rabbit was anaesthetized, bled, heparinized and then perfused with saline through the right jugular vein to the left carotid artery until the effluent was clear. Tissues were then each dissected separately with sterile instruments, ground up and inoculated intracerebrally into young adult mice. The virus in the blood fell from 2·3 log LD50 on the 1st day to 1 log on the 2nd and virus was not detected thereafter. In the regional lymph nodes virus was detected up to the 6th day: 3·5, 3·3 and 2 log LD50 in the first 3 days. In the para-aortal nodes the titre fell from 2·5 log 1 day after inoculation to 1·5 log on the 3rd day, after which none was detected. 1·3 log was detected on the first 3 days in the mesenteric nodes and 2·2–2·6 log on the same days in the spleen.

C. E. Gordon Smith

ERRATUM

The Editor regrets that owing to a misunderstanding an editorial comment was made in the abstract of a paper by SALMINEN *et al.* [this *Bulletin*, 1961, v. 36, 612], and incorrect values were given on fatty acids and other substances, millimoles being quoted instead of micromoles.

The abstract should read as follows:—

SALMINEN, A., RENKONEN, O. V. & RENKONEN, O. **Nature of Lipid Inhibitors of Tick-Borne Encephalitis Virus Hemagglutination. I. Inhibitory Lipids of Human Serum.** *Ann. Med. Exper. et Biol. Fenniae.* Helsinki. 1960, v. 38, No. 4, 447–55. [15 refs.] **II. Inhibitory Activity of Authentic Lipids and their Mixtures.** *Ibid.*, 456–64.

I. 4–8 units of haemagglutinin prepared by a sucrose-acetone extraction technique from the Belyanchikov strain of biphasic tick-borne encephalitis virus were used. Pooled human serum was subjected to Folch partition: 30% of the HI (haemagglutinin-inhibitor) activity of the original serum was in the chloroform phase (total lipids) and only traces in the aqueous phase. The total lipids were fractionated on silicic acid and HI activity (5–10% of original) was found only in the non-phosphatide fraction. This fraction was further fractionated and activity was found only in a fraction containing triglycerides + free fatty acids + free cholesterol but not in the individual components. When the mixture was fractionated on aluminium oxide the activity was lost but when the fractions obtained were mixed it was restored. Triglycerides + cholesterol and triglycerides + fatty acids were weakly active (1:4) but cholesterol + fatty acids strongly (1:128). The whole HI activity of the total lipids could be obtained by mixing the weakly active non-phosphatides with the inactive lecithin, sphingomyelin and lysolecithin in the proportions present in the total lipids. Free fatty acids, serum lecithins, sphingomyelins and lysolecithins are strong inhibitors only when mixed with free cholesterol but cholesterol esters and serum triglycerides were inactive even when mixed with free cholesterol.

II. Pure fatty acids and their esters, bile salts, and sterols and their esters, were non-inhibitory (1·6 μ-mole). Glycerophosphatides and sulphuric acid esters of long chain alcohols were non-inhibitory (0·2–0·4 μmole). Cardiolipin alone was inhibitory (2 μ-moles–1:256). 4 μmoles of even-numbered saturated fatty acids from C_{12} to C_{22} were inhibitory (1:16–1:32) when mixed with 10 μmoles cholesterol: but not C_6–C_{10} or C_{24}, C_{26}. The HI activity of C_{18} acids with 0–3 double bonds mixed with cholesterol was similar. With palmitic acid mixed with cholesterol HI activity increased with concentration to a plateau (1:64) at 8 μmoles and above: with increasing amounts of cholesterol a plateau is also reached. Methyl palmitate was inactive mixed with cholesterol but sulphuric acid esters of long-chain alcohols were active when so mixed. Bile acids mixed with cholesterol were about one-quarter as active as fatty acid mixtures. Glycerophosphatide cholesterol mixtures were as active as fatty acid mixtures and cardiolipin was 8 times as active. With palmitic acid only sitosterol of 3 sterols was active in replacing cholesterol. The results suggest that acidic groups are probably essential for activity and the hydroxyl groups on cholesterol may also be involved in the combination of inhibitor and haemagglutinin. *C. E. Gordon Smith*

LIBÍKOVÁ, H. **A Neutralisation Test with the Kyasanur Forest Disease (KFD) Virus in HeLa Cells.** [Correspondence.] *Acta Virologica.* Prague. 1961, May, v. 5, No. 3, 195.

A comparison was made of 3 neutralization tests with Kyasanur Forest disease virus: an intracerebral test in mice, a test in HeLa cells using cytopathic effect as the marker, and another using metabolic inhibition. Two hyperimmune sera against tick-borne encephalitis virus were tested and no significant difference was found between the methods. The formation of antibody in guineapigs inoculated with Kyasanur virus was demonstrated by a test with HeLa cells using cytopathic effect. *C. E. Gordon Smith*

SHOPE, R. E., CAUSEY, Calista E. & CAUSEY, O. R. **Itaqui Virus, a New Member of Arthropod-Borne Group C.** *Amer. J. Trop. Med. & Hyg.* 1961, Mar., v. 10, No. 2, 264–5.

Itaqui virus was isolated since 1956 from a patient with a mild febrile illness, from 4 sentinel monkeys, from 16 sentinel mouse groups and from a wild rat (*Proechimys*). It is pathogenic by all routes for adult and suckling mice. The average survival time in 3-day-old mice inoculated intracerebrally is 1 day, intraperitoneally 1·2 days, in adults inoculated intracerebrally it is 3·2 days. A haemagglutinin was prepared by acetone extraction of suckling-mouse serum. Neutralization tests were by intraperitoneal inoculation of 3-day-old mice. By haemagglutinin-inhibition and neutralization tests a relationship was demonstrated with Oriboca virus. By complement-fixation Itaqui was indistinguishable from Caraparu virus. Itaqui is thus the sixth member of group C. *C. E. Gordon Smith*

OKUNO, T. **Immunological Studies relating Two recently isolated Viruses, Germiston Virus from South Africa and Ilesha Virus from West Africa, to the Bunyamwera Group.** *Amer. J. Trop. Med. & Hyg.* 1961, Mar., v. 10, No. 2, 223–6.

2 strains of Germiston (SAAR 1050 and SAAR 1057) virus in their 4th and 1st mouse passages respectively, and 1 of Ilesha virus in its 5th mouse passage were used. Haemagglutinins and complement-fixing antigens were prepared mainly by sucrose acetone extraction of suckling mouse brain. The haemagglutinins reacted optimally at *p*H 6·0–6·2. Immune sera were prepared in mice. In cross haemagglutinin-inhibition tests with Bunyamwera and Cache Valley viruses, Germiston sera produced by two inoculations of virus reacted only with the homologous antigen but later sera reacted also in low titre with Ilesha, Bunyamwera and Cache Valley. Ilesha reacted with the homologous antigen and in lower titre with Cache Valley. Bunyamwera and Cache Valley sera reacted with all the heterologous viruses in lower titre than with homologous antigen. Kairi serum also reacted with all 4 antigens and Wyeomyia with Germiston and Cache Valley in low titre. Germiston appeared closest to Bunyamwera and Ilesha to Cache Valley on this basis.

In cross complement-fixation tests Germiston antiserum reacted only with homologous antigen, Ilesha serum reacted with Bunyamwera and Cache Valley as well as the homologous antigen. Bunyamwera serum reacted with all 6 antigens but most markedly with Ilesha and Cache Valley in addition to the homologous antigen. Cache Valley cross-reacted strongly with Ilesha and Bunyamwera and less with Wyeomyia. Kairi cross-reacted strongly with Ilesha and Bunyamwera and less with Cache Valley. Wyeomyia reacted with all, but strongly with Ilesha, Bunyamwera and Cache Valley. Thus in complement-fixation tests Germiston shows no strong cross-reactions but Ilesha appears to be close to Bunyamwera and Cache Valley. *C. E. Gordon Smith*

BÁRDOS, V., ADAMCOVÁ, J., BALÁT, F. & HUDEC, K. Serologické vyšetrenie vysokohorských vtákov na substancie neutralizujúce vírus Tahyna. Príspevok ku štúdii úlohy vtákov v ekológii vírusu Tahyna. II. **[Serological Examinations of Mountain Birds for Substances Neutralizing the Tahyna Virus]** *Československ. Epidemiol., Mikrobiol., Imunol.* Prague. 1961, v. 10, No. 3, 166–9. [10 refs.]

The English summary appended to the paper is as follows:—

"In the present work the authors investigated whether birds living in an altitude above 1,000 m. above sea-level [where the mosquito Aedes vexans is not found or only very rarely] who were shot and subjected to serological examination similarly as birds in the lowlands, have a substance neutralizing the Tahyna virus in the serum.

"Eluates from paper discs were prepared, using the method of Karstad et al. and examined for the virus by means of the neutralization test using young white mice according to Smithburn's method.

"Not in a single instance the presence of substances neutralizing the Tahyna virus was found. The number of examined birds was 67 including 51 full-grown ones and 16 young birds.

"The results are in agreement with those of serological examinations of the population and domestic animals in these mountainous regions and provide evidence that the circulation of the Tahyna virus on our territory is restricted mainly to areas with a mass incidence of Aedes vexans."

CAUSEY, O. R., CAUSEY, C. E., MAROJA, O. M. & MACEDO, D. G. **The Isolation of Arthropod-Borne Viruses, including Members of Two Hitherto Undescribed Serological Groups, in the Amazon Region of Brazil.** *Amer. J. Trop. Med. & Hyg.* 1961, Mar., v. 10, No. 2, 227–76, 7 figs. [20 refs.]

Results of the Belem laboratory from November 1954 to May 1959 are reported. The study area was in tropical rain forest at the mouth of the Para river. Viruses were isolated from the blood of 62 of 759 febrile patients working or living in the forest and from 2 of 565 febrile patients not in the forest. Viruses were also isolated from 144 of 230 sentinel monkeys (mainly *Cebus*) and 116 viruses from sentinel mice—adults or suckling groups. These represented 47 sentinel days per virus isolated from monkeys and 24 per virus for sentinel mice. From a total of 140,507 forest mosquitoes in 1,827 pools, 33 viruses were isolated. Arboviruses have also been isolated from 17 wild rats, opossums and sloths trapped in the area. The viruses were isolated by inoculation of mice 2–4 days old. A preliminary identification could be made on a basis of mouse pathogenicity and a dichotomous key is presented for the Belem viruses. Further identification depended on complement-fixation and neutralization tests.

Group A. Venezuelan encephalitis virus was isolated

from sentinel monkeys, mice and a rat, also from a wild rat (*Proechimys* sp.). It was also found in pools of *Haemagogus* spp., *Aedes serratus*, sabethines and mixed species. Monkeys were estimated to have an average of 4 days' viraemia. 5 of 6 human cases were mild febrile illnesses. Eastern encephalitis virus was isolated from 7 sentinel monkeys and from sentinel mice, all in the first 7 months of the year. Antibody has been demonstrated in man and horses in the area—clinical encephalitis in horses occurs between January and March in most years. Mayaro virus was isolated from patients with mild febrile illnesses.

Group B. Yellow fever isolations were previously described [*Trop. Dis. Bull.*, 1959, v. 56, 1228]. Ilheus virus was isolated from 2 patients with febrile illnesses —one of them had marked weakness of the limbs. One strain was from a sentinel monkey. One strain was from a pool of *Aedes* spp. (mainly *serratus*) and a second from a pool of *Psorophora ferox*. Bussuquara virus was isolated from sentinel monkeys and mice, from a pool of *Culex* (*Melanoconion*) sp. and from wild rats (*Proechimys* sp.).

Group C. This group has so far been isolated only in the Belem area where 200 strains have been obtained. Oriboca virus was isolated each year from man, sentinel monkeys and mice. It was also isolated from a pool of sabethine mosquitoes and 1 of *Mansonia* and *Psorophora*. The 2 patients had brief febrile illnesses. 22 of 150 human sera had antibody. Marituba virus was isolated from sentinel monkeys and from a patient with a febrile illness associated with dizziness and weakness of the lower limbs. Apeu virus was isolated from 3 patients with mild febrile illnesses and from sentinel monkeys. Murutucu virus was isolated from sentinel monkeys and mice, from trapped animals (*Nectomys* and *Bradypus*), from a pool of sabethine mosquitoes and from 2 patients with mild febrile illnesses. Caraparu virus was the most frequently isolated group C agent encountered. It was isolated from patients with febrile illnesses—1 of them associated with weakness of the legs for several weeks. It was also isolated from sentinel monkeys and mice and a pool of mosquitoes of mixed *Aedes* and sabethine mosquitoes.

Guama Group. More than 100 isolations comprising 2 viruses have been made. Both have an average of 6 days' viraemia in monkeys. Guama virus was isolated from 2 human patients with febrile illnesses, from sentinel monkeys and mice, from wild-caught rodents and from a pool of *Culex* (*Melanoconion*) sp. Catu virus was obtained from the same sources except mosquitoes.

Bunyamwera Group. 13 isolations in this group were made from mosquitoes: Cache Valley virus from a mixed pool of *Aedes, Mansonia* and *Psorophora*; Kairi virus from a pool of *Aedes scapularis*; and 11 strains of the Wyeomyia complex of viruses from 2 pools containing only *Trichoprosopon digitatum* and from pools of sabethines and *Aedes* species.

2 strains of one virus (Tr 9375) in the California complex were isolated; 1 from a pool of *Aedes scapularis* and the other from a mixed mosquito pool. 2 other strains were isolated from sentinel monkeys. One ungrouped virus (Tacaiuma) was isolated from a sentinel monkey.

[This highly condensed paper records very remarkable work and contains a wealth of important details which cannot be encompassed in an abstract.]

C. E. Gordon Smith

CASALS, J. & WHITMAN, L. **Group C, a New Serological Group of Hitherto Undescribed Arthropod-Borne Viruses. Immunological Studies.** *Amer. J. Trop. Med. & Hyg.* 1961, Mar., v. 10, No. 2, 250–58.

The viruses were studied at the 3rd to 8th passage in newborn mice. In mice viraemia of at least 8 log LD50 is reached in 48 hours with a similar concentration in the liver. The titre in brain is only 5–7 log LD50. Sera were prepared by intraperitoneal inoculation of mice or intracerebral inoculation of guineapigs. Haemagglutinins were prepared by acetone-ether extraction of newborn mouse serum. The optimum conditions were *p*H 6·0–6·2 at room temperature. For neutralization tests which were made in newborn mice, mouse serum virus was found most satisfactory. Complement-fixing antigens were made by acetone extraction of liver or sometimes brain of suckling mice. Haemagglutinin-inhibition tests showed that Marituba and Murutucu viruses were fairly closely related as were Apeu and Caraparu but the two pairs were easily separable from one another and from Oriboca virus. Cross neutralization tests between Marituba, Apeu and Oriboca viruses with hyperimmune sera in an intraperitoneal test showed strong cross-relationships between them all. With an intracerebral test cross neutralization tests showed closer relations between strains of Marituba and Murutucu, and between Caraparu and Apeu than between the pairs. Cross complement-fixation tests demonstrated little or no difference between Oriboca, Marituba, Murutucu and Apeu viruses. One strain of Caraparu (H5546) also showed a strong relationship but 2 strains (An 3994 and An 7981) appeared to be deficient in the common antigen. No antigenic relation was found between the viruses in this group and other grouped or ungrouped arthropod-borne viruses.

Antibody to group C viruses has been found in 0 of 60 human sera from Jamaica, 0 of 25 from Puerto Rico, 0 of 22 from Trinidad, and 0 of 40 from Hong Kong. 38 of 316 human sera from South, West and East Africa had haemagglutinin-inhibiting but, in the few tested, not neutralizing antibody to Oriboca virus. 52 of 77 sera from Belem had antibody to 1 or more group C viruses.

C. E. Gordon Smith

WHITMAN, L. & CASALS, J. **The Guamá Group: a New Serological Group of Hitherto Undescribed Viruses. Immunological Studies.** *Amer. J. Trop. Med. & Hyg.* 1961, Mar., v. 10, No. 2, 259–63, 1 fig.

About 20 strains from Belem were found to comprise 2 viruses—Guama and Catu. A related but different virus—Bimiti—was isolated from mosquitoes in Trinidad. They were maintained by intracerebral inoculation of newborn mice—they have only limited pathogenicity for adult mice although 1 strain has been adapted to them. The strains used were in their 3rd–10th mouse

passages. The sera of surviving inoculated adult mice were used. Haemagglutinins have not been discovered. Neutralization tests were made by intracerebral inoculation of newborn mice. Complement-fixing antigens were made by acetone-ether or sucrose-acetone extraction of newborn mouse brain. Haemagglutinin-inhibition tests with Guama group antisera and antigens of other arthropod-borne viruses revealed no relationship. Neutralization tests clearly distinguished Guama and Catu viruses. With hyperimmune sera greater cross-reactions could be demonstrated between Guama, Catu and Bimiti viruses. In cross complement-fixation tests each antiserum reacted equally well with each antigen with the possible exception of Bimiti which was slightly more reactive with its own antigen than with the others. Cross complement-fixation tests with a variety of grouped and ungrouped arthropod-borne viruses revealed no relationship.

C. E. Gordon Smith

BEN-PORAT, T., REISSIG, Magdalena & KAPLAN, A. S. **Effect of Mitomycin C on the Synthesis of Infective Virus and Deoxyribonucleic Acid in Pseudorabies Virus-Infected Rabbit Kidney Cells.** *Nature.* 1961, Apr. 1, v. 190, 33–4, 1 fig.

When rabbit kidney cells in the stationary phase of growth were infected by pseudorabies virus, DNA synthesis (measured by uptake of labelled thymidine) was stimulated; when actively growing cells were similarly infected DNA synthesis was reduced (KAPLAN and BEN-PORAT, *Virology*, 1960, v. 11, 12). The addition of mitomycin C to young or old cultures was found to inhibit DNA synthesis without affecting RNA synthesis (measured by uptake of labelled uridine). With old cultures treated with mitomycin C, this inhibition was reversed by pseudorabies virus, DNA synthesis still being stimulated immediately after infection. Young cultures treated with mitomycin C and then infected did not recover the ability to synthesize DNA. The yield of infective virus from old cultures treated with mitomycin C was very low, but the same numbers of virus particles could be seen in electron micrographs as in control fluids from untreated cultures. Although these particles did not initiate the formation of plaques, they did give rise to intranuclear inclusions and to the characteristic cytopathic changes observed after infection with normally infective pseudorabies virus.

SEKIGUCHI and TAGAKI (*Biochim. et Biophys. Acta*, 1960, v. 41, 434) have obtained similar results with *Escherichia coli* treated with mitomycin C and infected by phages T2, T3 or T5, and they have interpreted them to mean that DNA synthesis in infected bacteria, which is not blocked by mitomycin C, proceeds by a different pathway from that in uninfected bacteria, which is blocked. The present authors suggest that in rabbit kidney cells in the stationary phase of growth, infection by pseudorabies virus is followed by the massive induction of enzymes concerned in DNA synthesis and that the rate of induction exceeds the rate of their inhibition by mitomycin C.

Janice Taverne

IMMUNITY

LEVINE, L., WYMAN, Louise, BRODERICK, E. J. & IPSEN, J., Jr. **A Field Study in Triple Immunization (Diphtheria, Pertussis, Tetanus). Estimation of 3 Antibodies in Infant Sera from a Single Heel Puncture using Agglutination Techniques.** *J. Pediatrics.* St. Louis. 1960, Dec., v. 57, No. 6, 836–43, 5 figs. [10 refs.]

Heel punctures on 140 infants yielding 0·1–0·2 ml. of serum which was diluted 1–20 and held in the frozen state made it possible to do estimations of pertussis agglutinations and of antibody to diphtheria and tetanus toxin provided the haemagglutination technique was used in the estimation of the antitoxins.

Variations of titre were closely related to dosage and lapse of time subsequent to immunization, and hence the methods are presumably reliable.

J. W. McLeod

BJORNEBOE, M. & JARNUM, S. **The Changes in Serum Proteins and Blood Volume during Immunization.** *J. Exper. Med.* 1961, June 1, v. 113, No. 6, 1005–11, 2 figs.

"In rabbits hyperimmunized with pneumococcal vaccine high concentrations of gamma globulin are produced. In such rabbits, plasma volume was determined with ^{131}I-labelled rabbit albumin and red cell volume with ^{51}Cr-labelled autologous red cells. It was found that the plasma volume increased with increasing gamma globulin concentration, the highest values observed being about 10 gm. per cent gamma globulin and about 70 ml. plasma per kg. as against normal values of 0·6 to 0·7 gm. per cent gamma globulin and 30 ml. plasma per kg. The red cell volume was the same in immunized and in normal rabbits and consequently hemoglobin concentration fell with increasing gamma globulin."

McGANN, Virginia G., STEARMAN, R. L. & WRIGHT, G. G. **Studies on Immunity in Anthrax. VIII. Relationship of Complement-Fixing Activity to Protective Activity of Culture Filtrates.** *J. Immunology.* 1961, Apr., v. 86, No. 4, 458–64, 3 figs. [13 refs.]

"Complement fixation reactions were obtained with rabbit antisera and culture filtrates or partially purified preparations of protective antigen of *Bacillus anthracis*. By selection of appropriate antisera and adjustment of conditions, fixation by heat-stable antigens of no protective activity could be minimized or eliminated,

Fixation titers were compared with the activity of the antigen preparations in active immunization of guinea pigs. A method was developed for deriving a dose-response curve from the mean reciprocal survival time after challenge of immunized guinea pigs. By use of this curve the results of the immunization assays were converted to relative potency units of protective antigen. There was significant correlation between the complement fixation titers and the immunizing activity of the preparations. The deviations were no greater than would be expected in view of the limited precision of the *in vivo* assay when practical numbers of guinea pigs are used. The significance of the results is discussed."

ROTHER, U. & ROTHER, K. Über einen angeborenen Komplement-Defekt bei Kaninchen. [**Congenital Deficiency in Complement in Rabbits**] *Ztschr. f. Immunitätsf. u. Exper. Therap.* 1961, May, v. 121, No. 3, 224–32, 1 fig.

The English summary appended to the paper is as follows:—

"Sera of six rabbits were shown to be deficient of complement activity in the haemolytic system. The defect is due to the absence of normal activity of the third component of complement and was found constantly over periods from eight weeks of age (first check) to 26 months."

Book Reviews

MACMAHON, Brian [M.D., Ph.D., D.P.H.], PUGH, Thomas F. [M.D., M.P.H.] & IPSEN, Johannes [C.M., Dr. Med., M.P.H.]. **Epidemiologic Methods.** 302 pp. 1960. London: J. & A. Churchill Ltd., 104, Gloucester Place, W.1. [55s.]

American epidemiology owes a great deal to the Harvard School and particularly to Professor John Gordon. This book, of which his successor is part-author, is essentially an elementary introduction to the techniques of epidemiology. It carries the subject from arguments about why epidemiology should be used at all in medical research to illustrations of the classic pitfalls in sampling, controlled studies and the interpretation of results.

The definition of epidemiology which is used: "The Study of the Distribution and Determinants of Disease Prevalence in Man", is broad enough to support an argument for a separate and distinct discipline of epidemiology with its own characteristic contribution to medicine. Further support comes particularly from the chapters on Cause, the Strategy of Epidemiology, and Analytic and Experimental Epidemiology.

The notion of the interaction of causes is notoriously difficult for medical undergradulates to understand. For the most part they are brought up with almost a one-cause-one-effect approach and a multiplicity of causes is as difficult for them to accept as is the notion of our duty to manipulate the environment in prevention. This recurrent problem of the real meaning of the associations which we demonstrate between disease and environment is faced early in the book, but the newer techniques which can help so much in our analyses of these associations are not mentioned.

Important among introductory chapters is a discussion headed: "The Strategy of Epidemiology" (pp. 32–50). The authors feel that the use of epidemiological techniques is obviously more rewarding at some stages in the attack upon a disease than at others. The timing and placing of the epidemiological contribution, for example, to the understanding of dental caries, must depend largely upon how much work had already been done by clinicians and pathologists upon the pathological process. It is rarely possible for a problem to be attacked only epidemiologically. Where a problem is attacked in this way definite stages of epidemiological study are discernible: First, the measurement of the occurrence of the disease in populations having different known characteristics; next, the formulation of hypotheses and their testing in special studies, and finally experimental studies on human populations. Dr. MacMahon takes each of these stages as a section in his book.

The measurement of the occurrence of disease in various populations involves the description of the conventional rates—prevalence, incidence, morbidity, etc. and there are several chapters on the different ways in which to classify populations. The Social classifications of income, occupation and Social Class which are so important to our own studies in Britain, are dealt with only briefly, as are the ethnic, regional and family classifications which seem to have more meaning in the United States than over here.

The testing of hypotheses—the authors call this "Analytic Epidemiology"—usually involves case history studies or studies over a period of time of a group or cohort in the population. Here the authors describe briefly the classical retrospective and prospective methods, but are chary of taking us much further than the most elementary idea of statistical significance.

The final chapter on experimental epidemiology describes various simple controlled and uncontrolled trials.

There is a good bibliography and an adequate index.

Epidemiology as a subject has paid such dividends in the last few years, particularly in unravelling the chronic diseases, that it has rightly received great and increasing attention. As the principal tool of workers in preventive medicine, it is now taught as a separate subject in a great number of universities. It is a young but particularly popular subject in America. Thus an introduction for American students and clinicians is of

great importance. Like all introductions, it should be easily understood and likely to increase interest as well as to inform and instruct. It seems very likely that the book will achieve this aim. However, for some of us this introduction will only whet the appetite. It leaves off where we wish it had begun, and it leaves us disappointed that the authors should have chosen to reach only this particular (though very important) group of students, rather than a wider public.

E. Maurice Backett

PEMBERTON, J. [M.D., M.R.C.P., D.P.H.] & WILLARD, H. [M.D.] [Edited by.] **Recent Studies in Epidemiology.** pp. xiii + 203, illustrated. 1958. Oxford: Blackwell Scientific Publications. [25s.]

This is a report in book form of a number of papers presented at the meeting in September 1957 of the Study Group on Current Epidemiological Research organized by the International Corresponding Club in Preventive and Social Medicine at Noordwijk aan Zee, Holland. The scope of the book is indicated by the following summary of sections:

1. The use of existing morbidity and mortality records in epidemiological research. 2. The *ad hoc* field survey, or getting your own data. 3. The evaluation of health needs and services by the epidemiological method, including applications to under-developed territories. 4. Applications of the epidemiological method to problems of mental health. 5. General practice as a field for epidemiology. Each section consists of a few contributions by experts from a number of British, North American and European countries.

In spite of the excellence of much of the material and the ability of both editors and contributors, this is a somewhat disappointing book. Other publications in the "recent advances" series have aimed at an authoritative account of selected work, which, though the results are generally accepted, is too late for inclusion in the standard text-books. The editors have had a well-nigh impossible task to fit their material to such terms of reference or to find any unifying concept in papers which present such a diversity of subject-matter, style and degree of detail.

A really satisfactory book on epidemiological research has probably yet to be written. Those which have appeared have usually succeeded to the extent that they deal with methodology, which is now well enough established to be described authoritatively and comprehensively, and avoid the systematic presentation of results, which can only embody a modicum of the current output of research, and which in any case are so likely to be equivocal in their interpretation or outdated by later work. The success of BRADFORD HILL's classic *Principles of Medical Statistics* [this *Bulletin*, 1955, v. 30, 931] is due as much as anything to its clear exposition of method and its avoidance of medical subject-matter except for strict purposes of illustration. The present book, by contrast, has the inevitable disadvantage of multiple authorship in that particular authors become identified with particular fields of study, so that the essential unity of method underlying their different contributions is forgotten in the concern of each to present a satisfying compendium of results. The subject-matter of epidemiology is as wide as that of medicine itself, so that this book covers a bewildering range of topics, ranging from cancer of the lung in nickel workers, through infective hepatitis in Czechoslovakia and institutional facilities for the mentally sick in Birmingham, to the study of three unusual conditions in the Caribbean.

While certain contributions are a delight to read, others lapse frequently into jargon, with which the subject is regrettably becoming riddled, and nowhere more so than across the Atlantic. Over-repetition of phrases such as "evaluation of health needs" and "the epidemiological method" can provoke an irrepressible yawn and a desire to skip to the next chapter. On the other hand, some pithy observations remain in the mind. A distinguished authority on hypertension is quoted as making "a strong case for choice of parents as the only effective preventive". In the case of the institutional facilities for the mentally sick, "those on the outside do not know the problems, those on the inside frequently cannot solve them".

Most of the material in this book has been reported elsewhere and it seems likely that the purpose of the original conference was not to present original work so much as a meeting of minds by discussion after each paper and by informal contacts between the participants. Printed without a reminder of the special context in which they were written, and without any account of the ensuing discussion, some of the papers seem emasculated and unsuitable for presentation in book form. The chapter on heart disease in Sweden, for instance, is only a cursory sketch of work undertaken or proposed by the contributor.

There is some overlap of both authorship and material with Witts's *Medical Surveys and Clinical Trials*, and it is a pity that these two books have appeared within so short an interval. If read selectively, however, the present book provides a stimulating account of a number of fields in which group methods of investigation have recently added to medical knowledge. In their excellent introduction the editors show themselves clearly aware of the pitfalls of such research.

A. S. Fairbairn

BROWNING, Ethel [M.D.] **Toxicity of Industrial Metals.** pp. vii + 325 + [14]. 1961. London: Butterworth & Co. (Publishers), Ltd., 88 Kingsway, W.C.2. [50s.]

The title of this book hardly indicates its scope. The metals are the principal ones met in modern industry—they are listed below—and they are surveyed from so many aspects that the book must be of value not only to those inside industry who are concerned with the working environment but also to doctors, physiologists, biochemists and other scientists in various fields and to students.

Metabolism is given special attention, after each of the 44 metals is described. Occurrence, the ores and alloys, important compounds, therapeutic agents, preparation, physical and chemical properties and the uses in industry appear in the beginning of each chapter. Each chapter's bibliography, with the author's flair for selection from the world's literature, should help research workers to the

ources of fully reported investigations, and her discussions show where fuller investigation may be necessary. The historical sequence in which the development of knowledge is presented builds up the picture and even though pioneer observations are shown as confirmed, disproved, enlarged upon or not yet fully understood, nevertheless the introduction of newer metals or their presence as by-products in the separation of older metals may lead to conditions harmful to health. Selenium and cadmium are given as examples of toxic metals increasingly used and falling into the familiar pattern of causing toxic effects in man before the degree of toxicity was recognized. Metal deficiency diseases in animals, birds and crops as well as the use of metals in therapeutics with effects good and bad and metal food contamination—all described where appropriate—might well, if known of by industrial technologists, have pointed the way to prevention of poisoning in industry. This gathering together of data is only one example of the book's general value.

Absorption and excretion, distribution and storage of metals in the organism and the accounts of metabolism show how toxic effects can be prevented and also how and where they can occur. The radioactive metals, which may enter the body from accident or nuclear fall-out, are not dealt with as such, but experiments with labelled metals to elucidate metabolic behaviour are described. Quantitative results are given as well in the sections on experimental animal physiology and toxicity before the accounts of human poisoning.

In the future editions which almost certainly will be necessary the few misprints, the meanings of which are clear, should disappear and perhaps there would be room for fuller accounts of therapy and prophylaxis. Chelation is explained and discussed in various parts of the book, indexed under the heading of versenate, in accordance with views reported by 1959. (A footnote to the excellent chapter on aluminium records the 1959 case of pulmonary fibrosis from exposure to aluminium dust in Britain [this *Bulletin*, 1959, v. 34, 906].) Since then more has been reported on the potential dangers of EDTA for example, but also of the usefulness of chelates in dealing with emergencies or potential tragedies: as usual, all such treatment or prophylaxis should be regarded as a calculated risk. There are inevitably some repetitions and perhaps dermatitic lesions are described in too much detail, though not so for the student.

Metals not described are calcium, sodium and potassium because of their relatively slight importance in industrial toxicology; nor is phosphorus, as the preface says, a highly toxic industrial agent but defined according to the Oxford New English Dictionary as a "non-metallic element"; nor is iron.

The metals described are: aluminium, antimony and stibine, arsenic and arsine; barium, beryllium, bismuth, boron and boranes; cadmium, cerium, cesium, chromium and chromates, cobalt, columbium and copper; gallium, germanium, indium, lanthanum, lead and tetraethyl lead and lithium: nickel and nickel carbonyl; magnesium, manganese, mercury and its compounds and molybdenum; osmium, palladium, platinum, rhenium, rhodium, rubidium and ruthenium; selenium, silver and strontium; tantalum, tellurium, thallium, tin and its organic compounds, titanium and tungsten; vanadium, zinc and zirconium.

M. Patricia Fitzsimons

MINISTRY OF AGRICULTURE, FISHERIES AND FOOD. **The Mites of Stored Food** [HUGHES, A. M.]. *Technical Bull.* No. 9. pp. vi + 287, 385 figs. 1961. London: H.M. Stationery Office. [17s. 6d.]

This book is a worthy successor, with expansion and rearrangement based on new knowledge, of *Mites Associated with Stored Food Products* [this *Bulletin*, 1948, v. 23, 1012] published by the same author in 1948. It is, like its predecessor, recognised by the scientific staff of the Ministry of Agriculture, Fisheries and Food as the standard reference work for the systematics and identification of those many species of mites which may actively infest, or be found in, stored products and concerning which it may be necessary to recommend control measures, or decide on the origin of an infestation. The new data have required changes in the arrangement of the subject matter and in nomenclature. But, long established names, *e.g. Pediculoides ventricosus*, are included in the index (to genera and species) and lead one to the newer name in the appropriate part of the text, in this instance, *Pyemotes ventricosus*.

Over half the book deals with the sub-order Sarcoptiformes which contains such acarines as the flour mite, cheese mite and related forms in a considerable classification. A relatively short section on the sub-order Trombidiformes includes *P. ventricosus*, etc., and predatory mites which accompany them. In the other major group, sub-order Parasitiformes or Mesostigmata, are considered at moderate length those mites of interest to workers on stored product infestation and which are of relatively appreciable size and closest to the ticks and blood-sucking mites, well known in the medical and veterinary spheres. Except where a species may cause dermatitis in persons handling infested products, acarines of medical and veterinary importance are, of course, not included in this work.

The main subject matter is preceded by an introductory chapter on mite anatomy relevant to taxonomy, and a review of classification which neatly puts in focus the various major groupings of mites, including the more important medically interesting forms not within the intention of this valuable book. The several sections within the book are well introduced by similar anatomical and taxonomic guides relevant to the sections. Keys are quite numerous and the descriptions well supported by nearly 400 excellent line drawings. Descriptive matter under species gives some synonomy, diagnostic description of one or more stages, biology and world distribution. An appendix deals with methods of examining material, culturing free-living mites, and—including formulae—with the making of permanent preparations. There are about 120 references.

D. S. Bertram

GUNSALUS, I. C. & STANIER, Roger Y. [Edited by.] **The Bacteria. A Treatise on Structure and Function. Vol. II. Metabolism.** pp. xv + 572, illustrated. 1961. New York 3. Academic Press Inc., Ill., Fifth Avenue, N.Y. London: 17, Old Queen Street, S.W.1. [$15.00]

Volume II of *The Bacteria* describes the energy-liberating systems of the bacterial cell and prepares the way for volumes III and IV which will deal with Biosynthesis

and Growth respectively. In view of the high standard achieved in the first volume of this work [this *Bulletin*, 1961, v. 36, 418], which was concerned with the structure of the bacterial cell, a valuable and impressive coverage of the subject was to be expected; and this expectation has been amply fulfilled.

The book contains 11 chapters, and the editors are to be congratulated on once again obtaining the services of an imposing list of contributors. The reader could hardly wish for a more authoritative statement of present-day knowledge in this field. I. C. GUNSALUS and C. W. SHUSTER (pp. 1–58) contribute the first chapter in which they discuss energy-yielding metabolism in bacteria, W. A. WOOD (pp. 59–149) writes on fermentation of carbohydrates and related compounds, H. A. BARKER (pp. 151–207) on fermentations of nitrogenous organic compounds, L. O. KRAMPITZ (pp. 209–256) on cyclic mechanisms of terminal oxidation, H. J. ROGERS (pp. 257–318) on the dissimilation of high molecular weight substances, M. I. DOLIN (pp. 319–363) on survey of microbial electron transport mechanisms, Lucile SMITH (pp. 365–396) on cytochrome systems in aerobic electron transport, J. W. NEWTON and M. D. KAMEN (pp. 397–423) on cytochrome systems in anaerobic electron transport, M. I. DOLIN (pp. 425–460) on cytochrome-independent electron transport enzymes of bacteria, D. M. GELLER (pp. 461–478) on bacterial photo-synthesis and W. D. MCELROY on bacterial luminescence (pp. 479–508).

The exceptionally clear system of sub-heading used in Volume I has been continued and again contributes greatly to readability and to the ease with which information can be located. Contributors have been allowed considerable freedom in scope and treatment and the reader is presented with an interesting and valuable variety of viewpoints and approaches to basic problems. Bibliographies are well constructed and provide a useful lead in to the more specialized literature. The successful description of enzyme reaction patterns depends to a large extent on the presentation of formulae and schematic diagrams. These are well done and will constitute one of the book's most valuable features.

A book of this size and scope cannot usefully be compared with any other existing publication on microbial metabolism. It will be of interest and value to the biochemist and the microbiologist, to the research worker and to the advanced student. The research worker particularly will benefit from the exposition of the many gaps and incongruities in knowledge mentioned by the editors in the preface and emphasized repeatedly in the text.

This book can be recommended as an outstanding, very detailed yet readable account of present knowledge of the energy-yielding metabolism of micro-organisms. If this standard is maintained through the remaining three volumes of *The Bacteria* the editors will have accomplished a monumental task and placed themselves heavily in the debt of microbiologists. *John R. Norris*

Notice

Consideration has from time to time been given to the question whether it would be desirable to include authors' addresses in the headings of abstracts in the *Bulletins* and it has been decided that the additional time and cost involved would not be justified. Subscribers are advised, however, that the Bureau will, on request, notify them of the name and address of the author of the article, or the publisher of the journal, from which an abstract has been made.

The Bureau also deals with enquiries from individual subscribers relating to abstracts which have appeared in the *Bulletin of Hygiene* and the *Tropical Diseases Bulletin*; correct references and the exact nature of the information required should be stated.

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